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Technology Review

MIT's Magazine of Innovation

★ *Special Issue*

10 EMERGING TECHNOLOGIES

They're raw. But they'll transform the Internet, computing, medicine, energy—and more. p43

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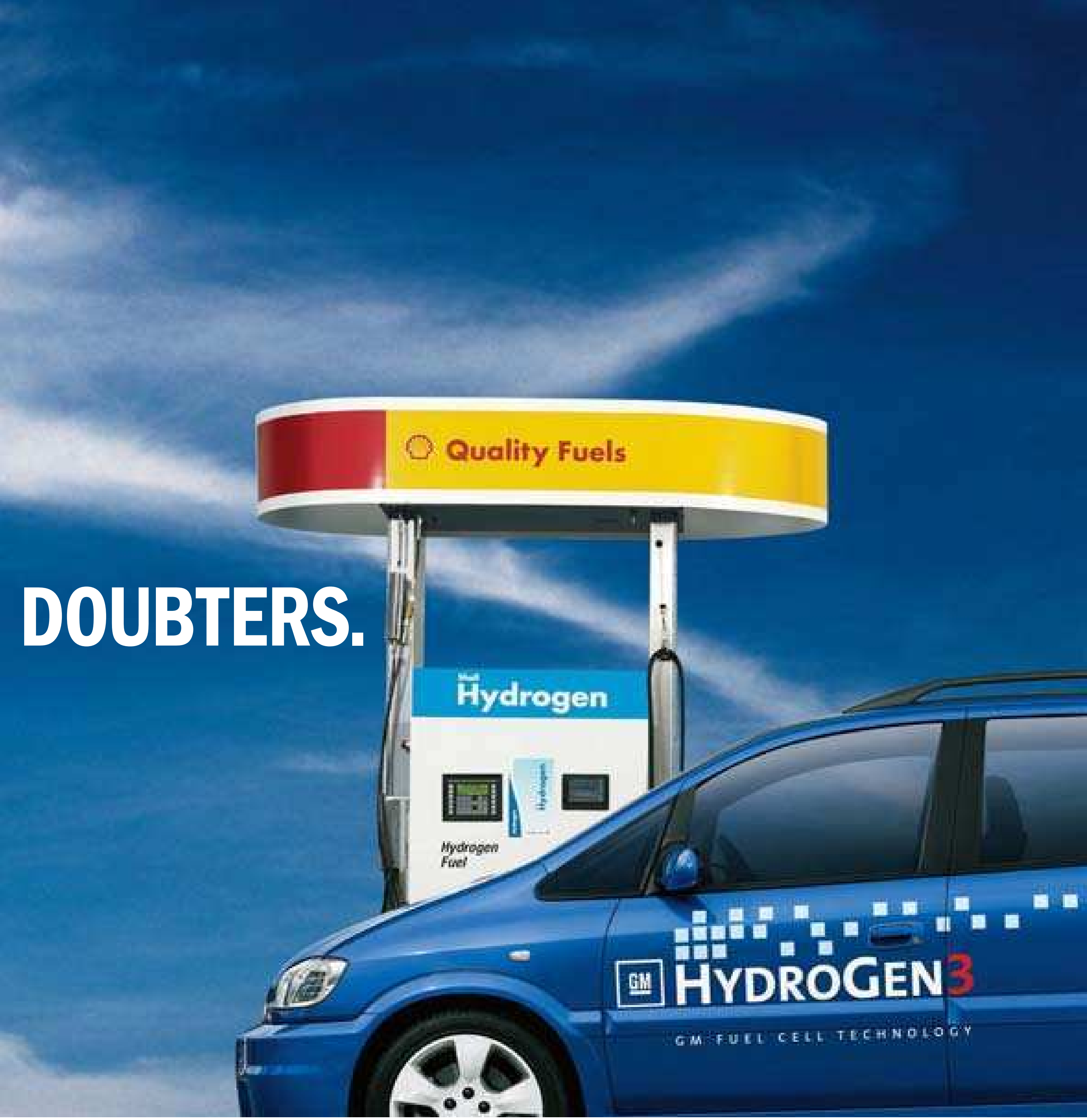

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Volume 108, Number 5

10 Emerging Technologies

Of the numerous technologies now in gestation at companies and universities, we have chosen 10 that we think will make particularly big splashes. They range from bacterial factories to silicon photonics to quantum wires—and any one of them could change your world.

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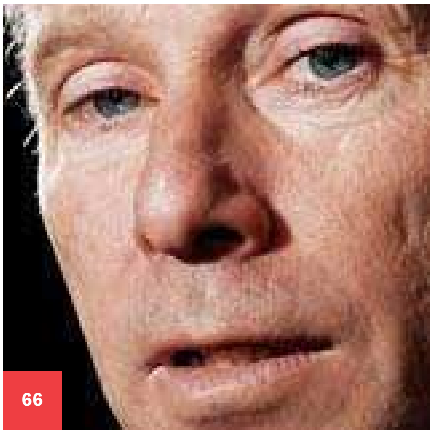

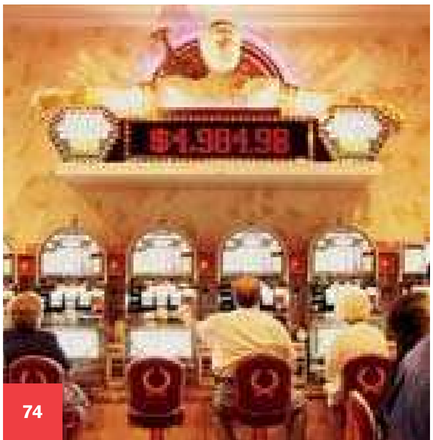

What's new at technologyreview.com

For the fourth year, *Technology Review* has chosen 10 emerging technologies that our editors believe will change the world. How have our past picks turned out? We were curious, and thought you might be too.

On our website, Stu Hutson gets us up to date on the latest news in grid computing, digital rights management, RNA interference, nanowires, biometrics, flexible transistors, and glycomics.

Plus: Charles Ferguson, who wrote our January 2005 cover story "What's Next for Google?", got so much thought-provoking feedback from *Technology Review* readers that he decided to further explore Microsoft's role in the digital world. (In his magazine piece, he contended that Google ought not underestimate Microsoft.) Ferguson is an entrepreneur who, in 1995, sold Vermeer Technologies to Microsoft for $130 million.

About Technology Review *Technology Review*, the oldest technology magazine in the world, is published by Technology Review, Inc., an independent media company owned by the Massachusetts Institute of Technology. Founded in 1899, *Technology Review* describes emerging technologies and analyzes their commercial, economic, social, and political impact for an audience of senior executives, researchers, financiers, and policymakers, as well as for the MIT alumni. In addition, Technology Review, Inc. produces technologyreview.com, a website that offers daily news and opinion on emerging technologies. It also produces live events such as the Emerging Technologies Conference. The views expressed in *Technology Review* are not necessarily those of MIT.

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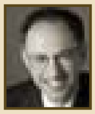

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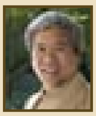

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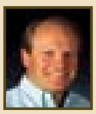

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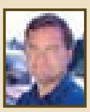

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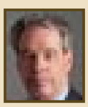

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The Rules of Innovation

Any sufficiently radical invention seems ridiculous to most people when they first encounter it. This is a rule of technological innovation.

In 1998, I ate lunch with an entrepreneur at a vegetarian restaurant in San Francisco. The entrepreneur, an ascetic and a yogi with startling blue eyes, spooned a lone bowl of bean soup and told me, "Software is a living tree." He said he had invented a new kind of software called PowWow that "would allow people to run in tribes on the Internet." He boasted that Tribal Voice, his new venture, would be the physical manifestation of what Indian shamans call "the golden thread." I was nonplussed.

Yet Tribal Voice could not be immediately dismissed, because the entrepreneur was John McAfee, the founder of the antivirus company McAfee Associates, for some years the most profitable company on earth. In 1989, when McAfee Associates was starting up, its business seemed as ridiculous as Tribal Voice did in 1998. It gave away its most important program, VirusScan, and sold licenses and support to corporations. This idea had made John McAfee supremely rich.

John McAfee's entrepreneurial career suggests another rule of innovation: the first attempt to commercialize an invention almost never succeeds.

McAfee conceived of his first company after posting free antivirus software on electronic bulletin boards. This "freeware" was very popular: computer users could download and use it without worrying about infringing copyright. Although information technology managers never planned it, the computers they managed were soon protected mainly by VirusScan. McAfee's great insight was that corporations would buy expensive licenses and premium services for free software their employees were already using. This innovation became the business model of the Internet and today is employed by most software companies.

Tribal Voice was equally inventive. PowWow allowed computer users to instantaneously communicate with other users with similar interests. From 1994 to 2001, more than eight million people congregated in "tribes" using PowWow. Tribal Voice was arguably the first social-networking company and among the first to distribute a multiprotocol instant-messaging (IM) program–that is, software that works with multiple IM standards and providers so that anyone registered with Yahoo's instant-message service, say, can exchange messages with buddies at AOL. Tribal Voice raised $10 million from Summit Partners in Palo Alto, CA, and TA Associates in Boston, MA; was purchased by CMGI, a services company, in Waltham, MA; and was distributed by AT&T and FreeServe as their preferred instant-messaging software.

But John McAfee's entrepreneurial career suggests another, less happy rule of innovation: the first attempt to commercialize an invention almost never succeeds.

There are two reasons for this. First, the innovator is often early: the really important market for the invention does not yet exist. Second (the point is related), the innovator doesn't know how to make money from the invention: the business model that will support the invention is imperfectly understood. Usually, therefore, another organization succeeds where the innovator failed. This is sometimes called the Second-Mover Advantage.

There are many examples of this advantage. Apple invented the Newton, but Palm successfully commercialized the personal digital assistant. Microsoft didn't create the personal computer, but because the company controlled the "platform" for software, it benefited most from the PC.

John McAfee's two companies nicely conform to this rule. McAfee Associates profited from the freeware movement where the first, countercultural freeware developers did not. But Tribal Voice collapsed in early 2000 when AOL, a mortal enemy of CMGI, blocked PowWow traffic completely, thereby isolating PowWow users from the largest community of IM users.

Tribal Voice was the innovator in two emerging markets, now much in the news, whose dynamics are still only partially known. The first is multiprotocol IM. The second is social networking. Today, thriving companies like Cerulean Studios and LinkedIn can be found in both markets. But John McAfee was there first, even if he didn't know how to make money from Tribal Voice.

John McAfee's inventions were maddeningly difficult to judge. This was not only because of their novelty. He was unable to describe his businesses except in New Age aphorisms. He liked to say, "Software wants to be free." But Walter Kortschak, the venture capitalist at Summit Partners who invested in Tribal Voice, thought McAfee was a canny old hippie. He once told *Red Herring*, the magazine I used to edit, "John has an incredible appreciation of how to make money. The rest is just bull…."

Today, McAfee practices yoga at his several homes in Hawaii and Colorado. Do you believe in the Second-Mover Advantage? Write to me at jason.pontin@technologyreview.com. ■

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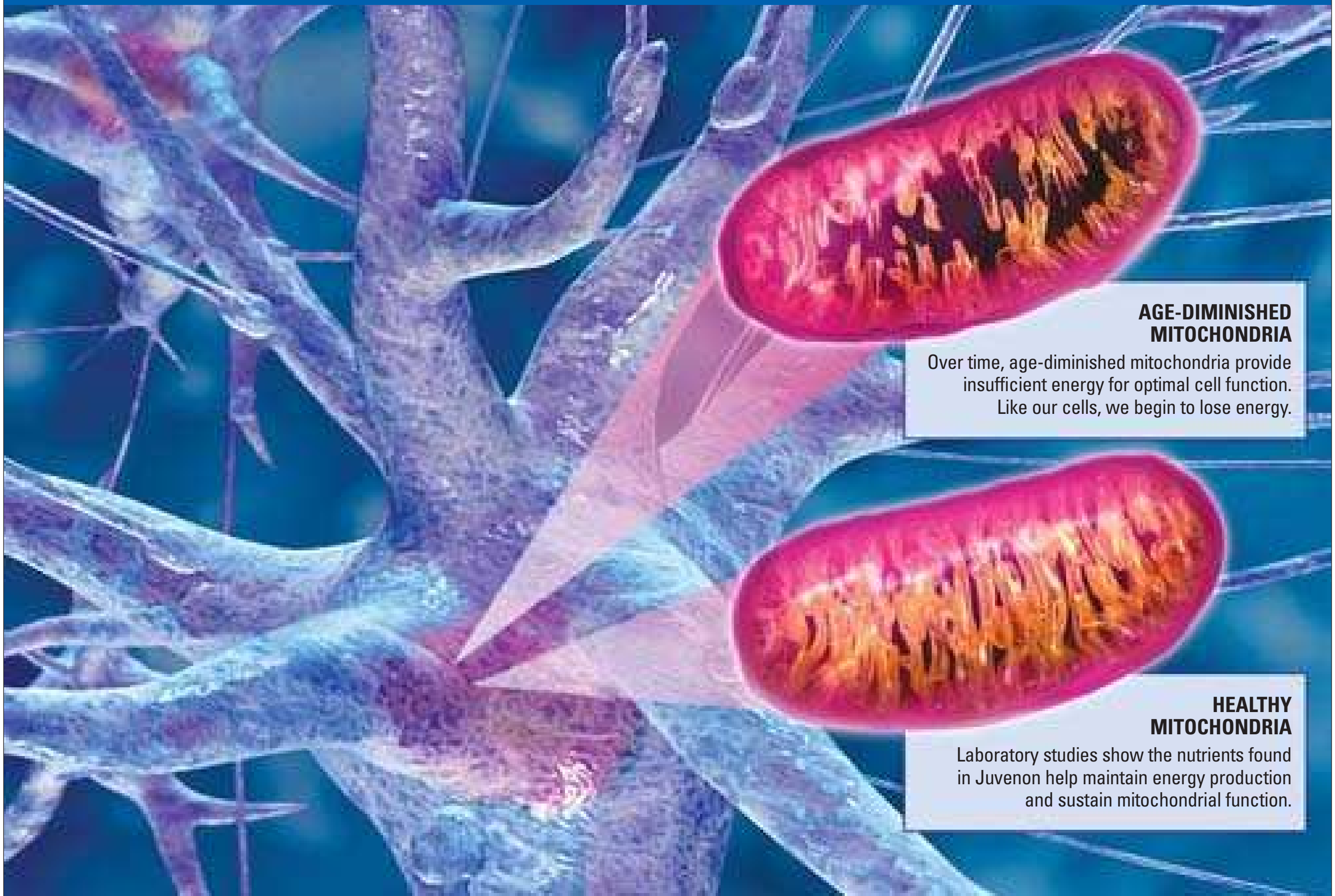

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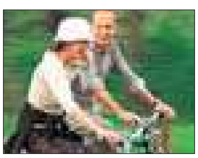

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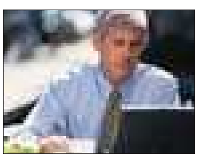

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Letters

FOLLOW THE MONEY

Jason Pontin's editorial "The Crisis in Tech Finance" (March 2005) brings out an important point about the so-called transfer gap between lab R&D and commercial financing. Your suggestion on using demand pull—with government creating demand for technologies before the market does so—is very useful. Unfortunately, it would be difficult to persuade those on the demand side to make such commitments without knowing that the technology offers a good solution to the problem at hand—and if it does, private financiers would probably be more than willing to back the technology anyway. The solution here could well be on the supply side: how far can the researchers push the technology with incremental innovation to make it visibly useful to the financiers?

Aditya Watal
New York, NY

Your editorial reads as if the baseline for "normal" investment in emerging technologies was set four years ago—with everything dropping from that point. Just as firms like Moody's look across an entire credit cycle before rendering an opinion, it would be helpful to put the funding trends you observed over the past three or four years into a broader context. Otherwise, the data is measured against a high-water mark set by the proverbial 100-year flood. It has nowhere to go but down.

Bryan McAllister
Allentown, PA

Pontin asks whether the "purchase commitments" with which the U.S. government has supported defense-related technology might work for other technologies as well. The answer is yes: the only things that stand in the way are ignorance and the lack of a national policy that encompasses an economic vision beyond sustaining a consumer-oriented marketplace. Starting around 1960, I spent 40 years in R&D at various federal agencies, including NASA and the Department of Defense. Ever since the early 1980s, it has been impossible to get a government agency to step up to the responsibility of reconciling the supply-demand curve. Even when it is recognized that the cost of introducing a product into the market is prohibitively expensive for private industry, the government has failed to respond. Meanwhile, private financiers show no desire to look beyond the next three to five years—they are eating the seed corn.

William D. Montjoye
San Antonio, TX

As an entrepreneur, it is my experience that venture capitalists are looking for a sure thing. This raises two questions. Why would someone with a "sure thing" want funding? And because low-risk investments translate into low returns, how were these venture capitalists going to deliver the high returns that they had promised their clients?

Arun Muralidhar
Chairman,
Mcube Investment Technologies
Plano, TX

HAIL RUSSIAN ENGINEERING

Ed Tenner's column about the AK-47 and Russian engineering ("Kalashnikov's Gun," March 2005) jolted my memory of combat in World War II. During the 1944 Warsaw Uprising, we had an assortment of submachine guns, including the homemade Blyskawica (Lightning), the German Schmeisser, the British Sten gun, and the Russian Pepesza. The German and British weapons had a very fine finish, while the Russian Pepesza had rough, unfinished external welding. When subjected to dirt and mud during combat, though, the Sten guns and Schmeissers jammed. The Pepesza withstood rough handling without failure.

Janusz Sciegienny
Newton, MA

Your article about the AK-47 reflects upon the Russian approach to technology—or rather the durability of it—in war. It is interesting to note that during World War II, the Russian engineers made sure their weapons and tank and truck fleets were standardized in less than half a dozen models or specs, unlike the Germans, who produced hundreds of unique vehicle, artillery, and weaponry designs, which resulted in a logistics and maintenance nightmare. The Russians produced a number of key items that were better than those of the Germans—superior tanks, sniper rifles, and optical sights, for example.

Marcus Gibson
London, England

SAVING THE WORLD WITH NUKES

Your summary of efforts to reduce the impact of greenhouse gas emissions on climate ("Engineering Climate," March 2005) left out what is still the most important "green" energy source: nuclear power. There is no economical and environmentally acceptable way to store wind or solar energy; the widespread applicability of biofuels is far from proven and may require unacceptable commitments of agricultural land; "clean" coal technology that emits no greenhouse gases is somewhere between a wish and a hope. In contrast, nuclear power is a proven means of large-scale electricity generation that eliminates hundreds of millions of tons of carbon dioxide emissions annually. Yet its future development is being stymied by political opponents who proclaim their horror at the threat of global warming. Solving the climate change problem without nuclear energy will be like running a marathon with lead weights attached to one's feet.

David C. Williams
Albuquerque, NM

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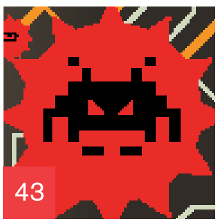
stripped to its logical bones.
Each concludes with a call to action.

INNOVATION

Vanquish the Cell-Phone Virus



Nine of the 10 technologies that we describe in this month's cover story *(see "10 Emerging Technologies," p. 43)* will make people's lives better in some interesting way. The 10th? Not so much. One of the wonders of the modern world, of course, is that nearly every person and apparently every electronic gadget can be connected. Wireless devices are taken for granted. Unfortunately, it turns out that these smart, connected gadgets can easily wreak electronic havoc. Virus programs, which have become an annoying fact of life for computer users, are now infecting cell phones, too *(see "Cell-Phone Viruses," p. 50)*. The impact will at first be minimal—your phone's address book might get scrambled, or you might find yourself billed for a series of phone calls you didn't make. But the potential for more-grievous harm is real, and it is very scary.

Americans used more than one trillion wireless-phone minutes in 2004, an increase of one-third over the previous year, according to CTIA, a wireless-industry trade organization. And as many have noted, cell phones will become our all-purpose tools for interacting with the digital world, regardless of our location. Increases in both wireless use and wireless capability multiply by many times the peril of a virus-infected cell phone. A corporate network fortified against wired assault may fall prey to a virus that hops from an employee's cell phone or PDA as it syncs to a desktop machine. An even greater threat is wireless malware that spreads via the Bluetooth protocol, worming its way into, say, a car computer. In that instance, the damage could be a corrupted GPS navigation system or something far worse.

This threat first materialized just last year, when a malicious cell-phone program, a worm called Cabir, was released in June as a sort of proof-of-concept exercise by a group of hackers called 29A. Since then, Cabir has morphed into at least 15 varieties, which have struck cell phones in 14 countries.

Computers fall prey to viruses in part because there is a single dominant software platform for them to attack. The first wave to hit cell phones targets the Symbian operating system. Fortunately, cell phones are not so homogenous as PCs; a bug that strikes Symbian phones still leaves many millions of others unscathed. But that's no cause for complacency. Symbian's market share is growing; in the fourth quarter of 2004, 53 percent of mobile devices sold worldwide ran on its operating system.

Wireless-service providers and cell-phone makers should get ahead of the threat. Just about every new PC comes preloaded with antivirus software; that needs to become the norm with mobile devices as well. The market would eventually demand it, but cell-phone vendors can take the first step by making such protection standard on all phones. Then maybe this latest digital scourge can be killed in its cradle. ■

BOOKS

The Death of Libraries?

Digitization of print could reduce today's libraries to musty archives.

At most libraries, the hand-typed card catalogues thumbed by generations of patrons have been supplanted by electronic indexes accessed via PCs locally or over the Web. Now that Google has agreed to scan millions of books from five major libraries and to make their contents searchable on the Web—a project that experts say is likely to yield spinoff technologies that drastically lower the costs of digitization and catalyze similar efforts worldwide—can the disappearance of libraries themselves be far behind?

Most librarians say no, as our story "The Infinite Library," on page 54, reports. Whatever the form in which book content is stored, librarians believe, people will still come to libraries for expert help finding information, for public access to the Internet, or for the comfortable atmosphere libraries provide for reading and reflection. And there will always be a need, professionals point out, for places that preserve traditional paper books.

All of that may be true. But there is still room to wonder how libraries will trump the expediency of being able to download a whole book over the Web, at little or no cost, instead of schlepping to the library. Print-on-demand services are spreading fast *(see "The Future of Books," January 2005)*, and electronic reading devices will continue to improve until they rival the resolution and usability of regular books. At that point, the only burning reason for a physical trip to the library will be to see a copy of a needed book that has not yet been digitized, or that has been digitized but is not downloadable due to copyright restrictions.

So in reality, the future of libraries may rest on just two factors: the rate at which digitization and display technologies advance, and the evolution of laws and practices regarding copyrights. In the United States, books published before January 1, 1923, are in the public domain and can be copied and redistributed by anyone, free of charge. At the same time, many books written in the past five to eight years have been published in both print and electronic form, and libraries have arranged with publishers to make some of these new e-books available for loan. (Borrowed e-books typically "expire," becoming unreadable after a certain period.) It's arranging access to the huge number of in-between books—those published between 1923 and the late 1990s—that is the critical issue.

If publishers and authors maintain their tight control on these books after they are scanned, public libraries will still have an important place as a free source for them, even if they can loan out only a few electronic copies at a time. On the other hand, if Google and others can arrange with publishers and authors to allow low-cost downloads of whole books—a likely prospect, seeing that it gives publishers a new way to squeeze revenues from their backlists—then libraries will inevitably recede in importance. It's a simple matter of convenience: free or low-cost access to digital books will make libraries more dispensable. Librarianship isn't about to disappear as a profession. But if librarians want a steady supply of patrons, they'll need to find ways to keep their institutions relevant in the digital age. ■

ENERGY

Fossilized Policy

Alternative electricity sources are ready; Washington is not.

Alternative energy technologies are increasingly effective—in terms of both technological soundness and economic competitiveness—and may soon mitigate some of the myriad geopolitical, health, and environmental problems rooted in our dependence on fossil fuels. Modern nuclear power plant designs reflect lessons learned from 50 years of reactor operation and could benefit from materials and control systems unavailable in the 1960s and 1970s. Wind turbines and, to a lesser extent, photovoltaics—solar cells that convert sunlight directly into electricity—are on the verge of competing more broadly against conventional sources of energy. Other technologies, like fuel cells, require more research but hold great promise.

All of the above, however, suffer from official neglect in the United States, which lacks a consistent national policy aimed at bringing alternative energy technologies into common use. The data, as shown in this month's "Data Mine" *(p. 30)*, tell part of the story. For example, President Bush proposes to spend just $84 million in solar-power research through the Department of Energy next year, while the figure for wind power stands at $44 million—less than one-sixth what he proposes to spend on coal-related R&D. Beyond this anemic R&D commitment to solar, the United States lacks a consistent, long-term plan to give renewables a more secure footing through initiatives like federal financing, tax credits, grid-connection mandates, and streamlined construction rules. This is too bad, because some of these technologies are ready for commercialization. Wind turbines, in particular, are efficient and reliable enough to compete against fossil fuels in some areas. The newest and biggest turbine prototypes—which we describe in "Wind Power Upgrade" *(p. 21)*—promise even better economics. Wind technology is ready to expand and with some federal help could do so quickly.

As for nuclear power, in the United States, innovative technologies languish, while overseas, plans to build new commer-

cial plants are gathering momentum. As Stewart Brand points out in “Environmental Heresies” *(p. 60)*, while one utility in the Carolinas talks about perhaps building an unspecified type of new nuclear plant someday in the future, companies in South Africa and China recently signed an agreement to collaborate on building two versions of the innovative “pebble bed” reactor. Brand notes that nuclear power plants don’t produce any greenhouse gases and are viewed by some experts as the best technology for producing the hydrogen we’d need to realize a “hydrogen economy.” But when we talk about nuclear power in the United States, it’s mainly to continue the endless arguments about where to put radioactive waste.

So where’s the government commitment to alternative technologies? It’s true that in March, legislators passed a bill that promotes the adoption of renewable electricity technologies. It includes a national fund to help pay for initial development, favorable lending and tax rates, and a requirement that electrical-grid operators adapt to renewable sources. Trouble is, the bill passed in China’s National People’s Congress. On Capitol Hill, an energy bill has been stalled for years, bogged down by controversial provisions, like one that would free oil companies of liability for health problems caused by a gasoline additive that has in some cases contaminated local drinking water.

With Washington offering no solutions, states have begun forming a patchwork of policies. Some states have enacted standards that require a percentage of electricity to come from renewable sources. And an association of western governors has called for more wind farms, among other clean energy sources. While these are encouraging developments, they are not a comprehensive strategy. Congress and President Bush should provide national leadership.

78

NEW ECONOMY

Banking on Technology

Looking at a prior Fed chief provides clues to why Greenspan got it right.

Correctly understanding how technology affects finance and business is vitally important for the welfare and prosperity of nations. And for nearly two decades, it may have been the most important part of Alan Greenspan’s job.

The departing chairman of the Federal Reserve Board of Governors is, of course, popularly linked with the “new economy” of the late 1990s—and with its awful consequence, the “tech bubble.” But as Roger Lowenstein, author of *Origins of the Crash*, explains in “How the Fed Learned to Love Technology” on page 78, the reign of the Fed chief, who will retire in January, coincided with a period of unprecedented innovation in information technology. When Greenspan took office in 1987, the PC was, for most consumers and businesspeople, just making its way onto the desktop, and the Internet was the province of a few hardcore technologists. That quickly changed. As the country’s top banker, Greenspan was responsible for understanding how technology was affecting the economy. He was forced to ask whether conventional economic rules were suddenly irrelevant. Specifically, he wondered, did technology allow productivity to grow faster than economists had previously thought—and help curb the risk of inflation?

In short, was there a new economy?

Greenspan’s answer was qualified: *kind of.* But on the most fundamental issue, concludes Lowenstein, Greenspan was right. The Fed chief suspected as early as 1996 that personal computers and networks had dramatically increased sustainable productivity growth. That supposition had profound policy implications: if it was correct, the U.S. central bank would have to abandon its long-time fixation on defeating inflation. Lowenstein describes how Greenspan’s predecessors, notably William McChesney Martin Jr., had spent much of their careers attempting to tame inflation. Martin, who was Fed chief from 1951 to 1970, had failed to do so. But if Greenspan was right about productivity, the Federal Reserve could allow the economy to heat up without raising interest rates. Indeed, Greenspan held interest rates steady, and as a result the economy continued to expand until 2000, while inflation remained low. By then, data showed clearly the productivity gains that Greenspan had assumed. As Lowenstein puts it, “Greenspan’s bet had nothing to do with dot-com stocks; he thought technology was making the rest of the economy—steel, finance, retail—more efficient. And so it was.”

Greenspan’s wrestling with the economic effects of information technology is just one example of how technology and economics are becoming ever more intertwined. Further illustrating the point, *TR*’s senior writer Gregory T. Huang explains in his review “The Economics of Brains,” on page 74, how a growing number of economists are beginning to use the tools of neuroscience, particularly brain imaging, to better understand how people make economic decisions. This research is in its early stages, but the preliminary findings are provocative. Some researchers, for instance, have identified the various parts of the brain that appear to be involved in different types of personal economic decisions. It may be that the “irrational exuberance” that Greenspan saw on Wall Street during the dot-com run-up was the result of investors’ thinking with a different part of the brain than they used when rationally devising strategies for their children’s college funds. Much still remains to be done. As Huang points out, “The challenge for economists lies in translating this sort of scientific insight into, say, predictive models of how people plan purchases or make retirement fund decisions.”

Most economists are becoming more savvy about information technology—and about innovation in general. At the same time, many still do not fully understand how newer technologies—in particular, innovations in biotechnology and medicine—will affect the economy in the future. It is essential that President Bush and his advisors, as they begin to think about a successor to the nation’s top banker, consider the importance of choosing a candidate who, like Greenspan, understands the critical role that technology plays in the nation’s economic life. Greenspan wasn’t always right about the new economy, but his faith in the power of technology paid dividends. We need a similar Fed chief for the 21st century. ■

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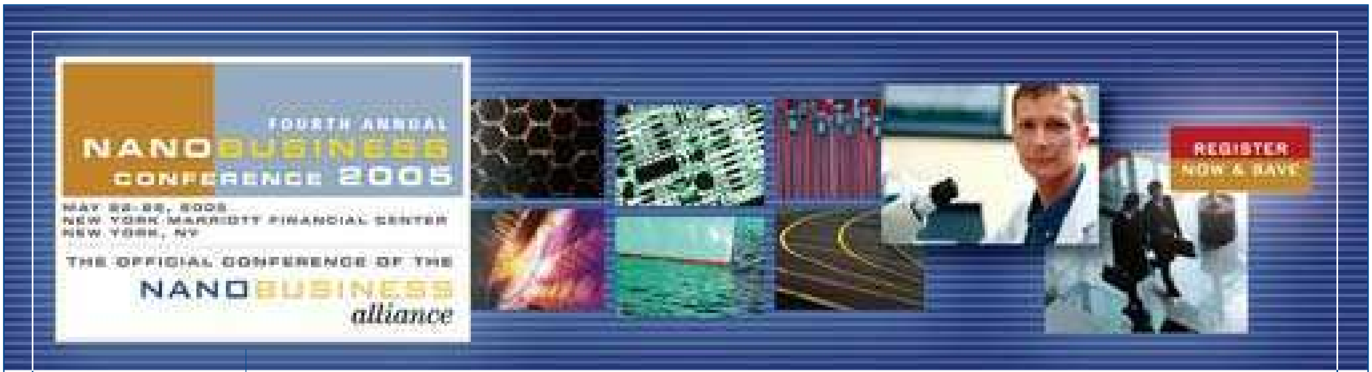

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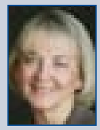
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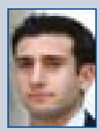
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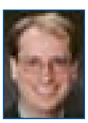
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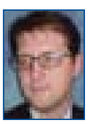
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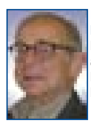
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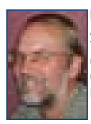
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"As corporations learn to take further advantage of our weaknesses, we may soon be asking for government to take on the role of protector and guarantor of our privacy, happiness, and savings."

Richard Anderson, psychiatrist and managing partner of Market Psychology Consulting, p. 76

"In a digital battlefield, once your position is known with accuracy, you're dead."

Roger McCarthy, chairman of engineering and scientific-consulting firm Exponent, www.technologyreview.com

"Google has brought us to a tipping point that could define how access to the world's literature may proceed."

Brewster Kahle, founder of the Internet Archive, p. 58

"We're screwed."

Bruce Schneier, founder and chief technology officer of Counterpane Internet Security, p. 50

"I think it will be quite profound to control my ankles again."

Hugh Herr, double amputee and head of the MIT Media Laboratory's biomechatronics group, p. 52

ENERGY

Wind Power Upgrade

Turbine technology looms large on the horizon

WIND POWER, ALREADY the world's fastest-growing source of electricity, is picking up still more momentum. The wind industry in Europe—the epicenter of wind power adoption—expects that one-quarter of the continent's new electricity-generating capacity in the next decade will come from wind. To both spur and serve this demand, manufacturers are developing colossal new offshore wind turbines with blade spans that exceed the length of a football field—including the end zones.

Today's largest commercial wind turbine has a blade span of 104 meters and produces up to 3.6 megawatts of electricity—enough to power 1,000 average U.S. households. But in February, Repower Systems of Germany switched on a demonstration turbine near Hamburg that produces five megawatts and has a blade span of 126 meters. And General Electric is developing a design for a 70-meter blade, which translates to a total blade span topping 140 meters. GE doesn't yet have a timeline for building such a massive machine but believes a turbine of that size could produce as much as seven

SHONAGH RAE

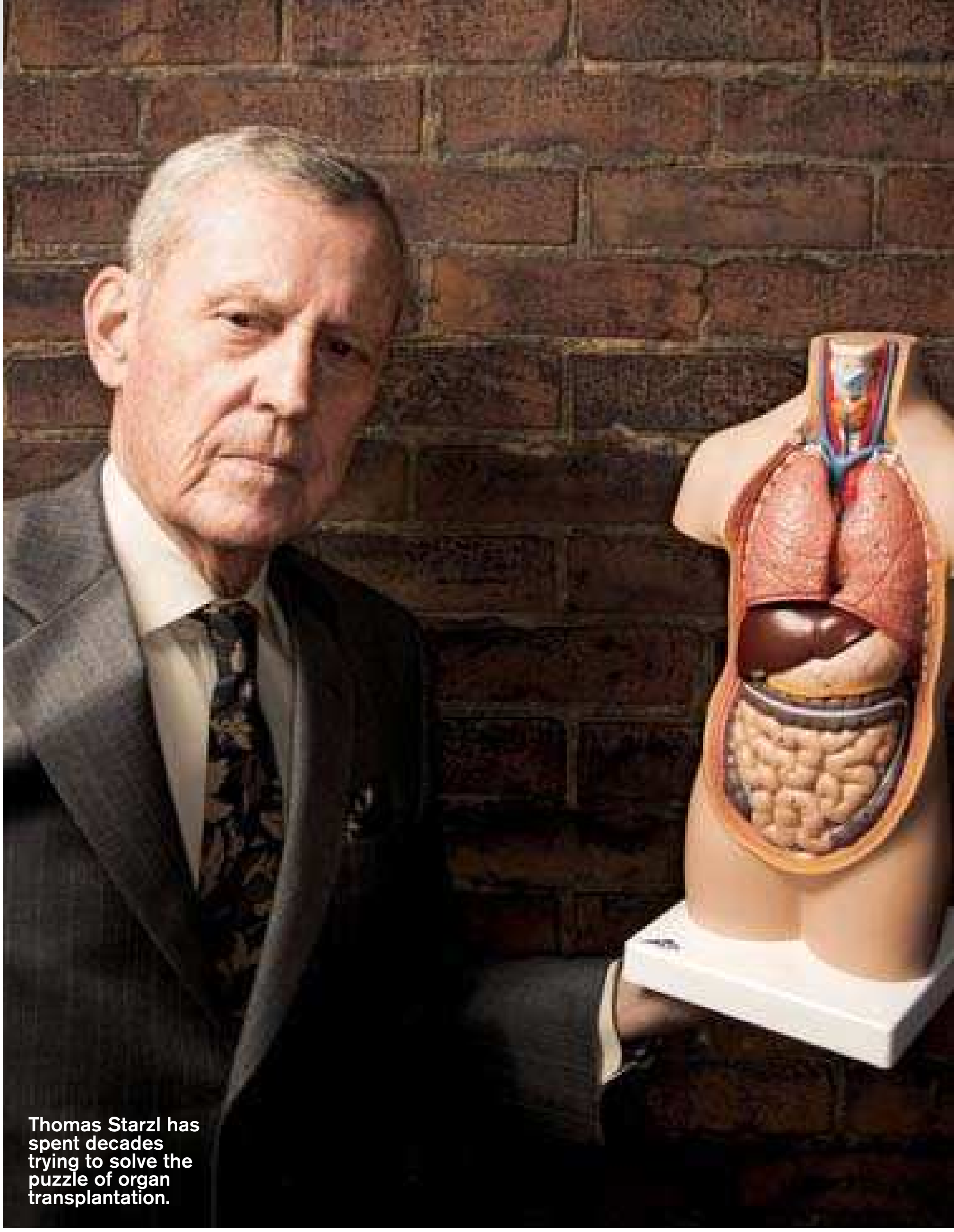
megawatts, says Jim Lyons, chief technologist at GE Wind.

"The economics work better as the turbines get bigger—and the name of the game is economics," says Bob Thresher, director of the National Wind Technology Center, a federal lab in Boulder, CO. The goal of industry and federal researchers is to create wind farms that produce electricity for about three cents per kilowatt-hour, down from about 4.5 cents today; that would beat the cost of fuel for the most efficient new gas-fired power plants—currently about 3.5 cents per kilowatt-hour. If the development process goes well, Thresher says, these huge turbines should be ready for widespread wind farm use in 2012.

If one turbine carries too large a portion of the power-generating load, and it fails, an energy company is going to lose its shirt.

Still, relying on superbig machines is not without risk, notes John McGowan, a mechanical engineer and wind energy expert at the University of Massachusetts Amherst. The bigger the turbines get, the higher the cost if one of them fails. "Sooner or later, they are going to make one too big," says McGowan, "and they are going to lose their shirt." And, he adds, efforts to develop turbines in the five- to seven-megawatt range are still too immature to yield reliable estimates of the cost of deploying them in wind farms.

Global wind power capacity grew 20 percent last year, and power-grid operators are wrestling with ways to integrate that increased output into today's transmission system. Bigger turbines churning out still more power would make solving that problem all the more critical. Wind farms' productivity fluctuates with the weather, and that's a challenge on the electrical grid, which must maintain a constant balance of supply and demand. Hydroelectric power, where available, can provide some stability. For example, last year Canadian Hydro Developers built a wind farm next to a hydroelectric plant in southern Alberta. Grid managers are also turning to advanced wind forecasts to help them plan ahead, tapping supplementary capacity or purchasing additional power as necessary. David Talbot



Thomas Starzl has spent decades trying to solve the puzzle of organ transplantation.

BILL CRAMER

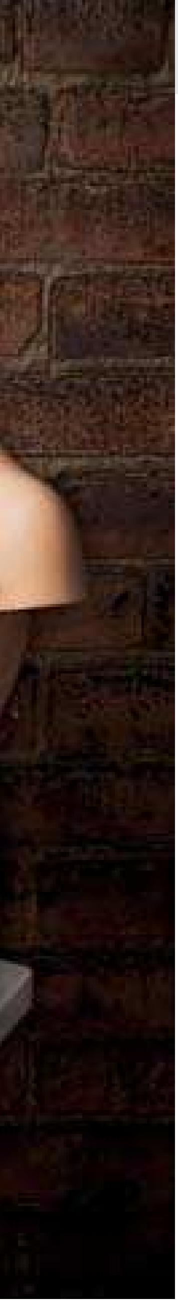
MEDICINE

Surgical Frontiersman

Transplant pioneer Thomas Starzl is still pushing medicine's boundaries

AT 79, THOMAS STARZL doesn't have much left to prove. In July 1967, the surgeon was the first to perform a successful human liver transplantation; since then he has been instrumental in making the liver the United States' second-most-commonly transplanted organ. "He led the field of transplantation into the modern era," says J. Richard Thistlethwaite, a transplant surgeon at the University of Chicago.

Despite his accomplishments and acclaim, though, Starzl still goes to work each day at the nation's most active organ transplantation center, a University of Pittsburgh facility that happens to be named after him. He and others in the field, it turns out, are still struggling with the same basic challenge they've faced since Starzl's pioneering surgeries: preventing patients' immune systems from attacking and destroying new organs.



That a field's founder is still doing battle with some of its oldest demons more than 40 years later is instructive. It reminds us that the birth of a new technology is not a discrete event, and that emerging technologies bring not only hope and new possibilities but also their own collections of emerging problems. That may be frustrating, but it's what drives many innovators and keeps them coming back to the office long after they really need to. "I'm pretending to be retired," says Starzl.

By the time Starzl began dabbling in liver transplantation in the late 1950s, doctors in Boston had already done the first kidney transplant. But because they had no form of drug treatment to prevent the immune system from rejecting an organ it recognized as foreign, they were limited to transplanting organs between twins. Most didn't think that transplanting organs between genetically dissimilar people was possible. But that didn't stop Starzl from trying.

Toiling alone in a hospital lab, Starzl, then 32 and a surgical fellow at Northwestern University, began by transplanting livers between dogs. At the outset, he didn't realize how bloody and difficult the procedure would be. All of the dogs died. Even so, he never thought of giving up. "I'm not sure I wasn't considered insane at the time," says Starzl. "It seemed a total fantasy."

But after gutting it out for nine years, and switching briefly to kidneys (which proved much easier to transplant), Starzl finally perfected his surgical technique and hit upon a combination of immune-suppressing drugs that kept transplant recipients, at least in the short term, from rejecting their new livers. Today, more than 5,000 Americans get new livers, and a new chance at life, every year. Immune-suppression treatments, many of them devised by Starzl, opened the door to other organ transplants as well and continue to improve. One-year survival rates for liver and kidney transplant recipients are now in the 85 to 95 percent range, up from less than 50 percent a few decades ago.

In developing immune-suppression therapies, though, Starzl and his colleagues traded one set of problems for another. Transplant patients on long-term suppressive regimens face higher-than-normal risks of infection, heart disease, diabetes, and kidney damage. And though immune-suppressing drugs effectively block acute rejection, many transplant recipients still suffer "chronic rejection," meaning that over time, their new organs begin to fail. All together, 20 to 30 percent of liver and kidney transplant recipients die within five years of their surgeries.

That a field's founder is still doing battle with some of its oldest demons more than 40 years later is instructive.

Starzl and other transplant researchers have therefore devoted themselves to finding more-sophisticated ways of training the immune system to accept new organs over the long term so that they can wean their patients off of the harsh antirejection drugs. One intriguing lead: a small number of transplant patients are "tolerant" of their new organs; they can stop taking the drugs, and their organs do just fine. Starzl's theory, a controversial one, is that a transplanted organ "sends its own army of cells out" into the recipient's body, and that in some cases, the peaceful coexistence of donor and recipient cells trains the immune system to accept the transplant. Giving patients immune-suppressing drugs *before* transplant surgery, Starzl argues, can help foster this coexistence; he's published evidence that such pretreatment reduces patients' need for immune-suppression therapy after surgery.

Even if Starzl is able to solve the problem of chronic rejection, though, that will do little to address another huge issue looming over transplant medicine: organ shortage. The next Starzl will likely be a pioneer in engineered "bioartificial" organs *(see "Saving Lives with Living Machines," July/August 2003)* or animal-to-human organ transplantation. And those technologies, of course, are almost certain to introduce a whole new set of challenges. Corie Lok

GETTY IMAGES

Prototype

Bling Booster

How do you make a diamond even more valuable? Tony Holden and Matee Serearuno, of the University of Cambridge's Institute of Manufacturing, believe they know. Their automated system for stonecutters, called iGem, works out the best way to cut a rough stone to maximize its value and reduce wastage. Descriptions of stones, which could eventually be derived from x-rays or surface scans, are fed to iGem, which classifies the stones according to size, shape, and clarity, based on variables identified by expert stonecutters. It then uses an optimization process to see, for example, whether the value of a borderline stone could be increased by a different cut that removes imperfections; in some cases, a smaller, clearer stone winds up being more valuable than a larger one. "Even small improvements can yield significant increases in profits," says Holden. In tests, the system boosted gems' value by up to 23 percent. The researchers' next goal is to integrate the system with a desktop x-ray scanner; they are discussing commercialization with a South African firm.

Keyboard Clues

Trying to use keyboard shortcuts in an unfamiliar software program is like trying to use a physical shortcut in an unfamiliar neighborhood: you're likely to get lost. San Jose, CA–based United Keys will soon release technology designed to make shortcuts—and therefore software—more usable. The startup is developing small liquid-

continued on p. 25

If the public pays for research, says Michael Eisen, it should be able to see the results.

TIMOTHY ARCHIBALD

PUBLISHING

Science Wants to Be Free

Open-access journals loose the chains

Publicly funded research belongs in the public domain, says Michael Eisen, a computational biologist at Lawrence Berkeley National Laboratory. Along with Stanford biochemist Patrick Brown and Nobel Prize–winning oncologist Harold Varmus, Eisen founded the Public Library of Science, which is launching three new "open access" scientific journals this year. The publishers of paid-subscription journals such as *Science*, *Nature*, and *Cell* aren't laughing.

What's the state of open-access publishing today?
Depending on who's counting, 95 percent of research papers in the life sciences are still locked up by the big commercial publishers—Elsevier, Springer, and the rest. It's ludicrous at a time when the Internet has pushed the actual cost of distributing a research paper close to zero.

But it's not as if a scientist who really needs a paper can't find it. Isn't that why research libraries pay for subscriptions?
For starters, if research were freely available, people would build better tools to sift through and dig things out. And what if you're Joe Guy who's just been diagnosed with cancer? It's ridiculous that you can't read papers that your tax dollars have paid for that might be pertinent to your condition. And often your doctor can't either—we won't even mention the doctor in Uganda. In the first issue of the *Lancet*—Elsevier's prime medical journal—there was an editorial stating that the aim of the publication was to communicate the findings of science to the widest possible audience. Somewhere along the line, they became a business and lost touch with why they exist.

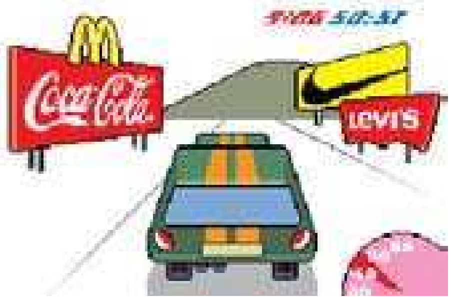
The latest policy from the National Institutes of Health "asks" grant recipients to submit their results for public access within a year of publication but doesn't require it. That's a lot less than some people were hoping for; what happened?
The forces of darkness surprised us.

"Forces of darkness"?
Scientific publishing is a $10 billion global business, growing 10 percent a year. They're not going to let go without a fight. The Association of American Publishers has hired [former congressperson] Pat Schroeder as its president and chief lobbyist—the queen of darkness. They went up to Capitol Hill and said we were socializing scientific publishing. NIH knows where its purse strings are.

Any merit to their argument?
It's ludicrous. What we have now is an egregiously subsidized industry—they're given content for free and then paid tremendous amounts of money to process and distribute it. Peer reviewers mostly aren't compensated. In a lot of fields, even the people who oversee the peer-review process are volunteers. And of course, the research that went into the papers is already paid for. And then the publishers have the gall to insist that they own a copyright on the results. Spencer Reiss

SOFTWARE

Advertisers: Game On

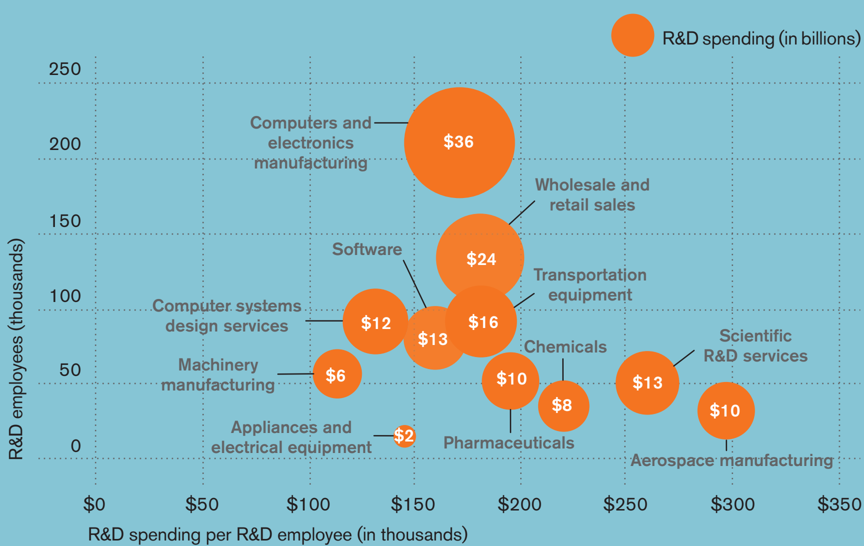


COMING SOON TO a video game near you: more ads. Last year, companies paid $200 million to place ads in games—a figure set to grow fivefold by 2008, according to market research firm DFC Intelligence. One reason for the projected jump in spending: new tools that could make ads in games more effective by tailoring them to players' ages or locations, or even the time of day that a game is played. With the technology, a player in Moscow, say, won't get a banner hawking a new Nike shoe that isn't available in Russia. Several firms, including Massive, inGamePartners, and Bidamic, unveiled such dynamic in-game advertising in late 2004. DoubleFusion of Jerusalem, Israel, takes the technology even further, presenting ads as video, audio, and 3-D objects woven seamlessly into games' virtual worlds. Developers using DoubleFusion's system insert code into their games that dictates where ads will appear. To prevent disruptions, they also specify when and how often the ads can be altered; DoubleFusion then updates the ads via its server. A player driving around a racetrack might pass a billboard advertising Tom Cruise's latest movie, hear Metallica's new single, or get extra points for driving over a Pirelli tire. The first DoubleFusion-powered game, London Taxi, from Data Design Interactive of Stourbridge, England, will be launched mid-2005. Tania Hershman

R&D

U.S. Corporate Research

One-fifth of the more than one million U.S. corporate and federal R&D scientists and engineers work on computer hardware and electronics. Another 16 percent develop software, design networked computer systems, or provide computer consulting, meaning more than one in every three U.S. corporate and government R&D employees works in information technology. Industries often considered R&D intensive, such as pharmaceuticals and aerospace, actually employ comparatively fewer workers and spend less overall. Aerospace companies, however, spend the most per worker.



R&D SPENDING DATA IS FROM 2002 AND EXCLUDES R&D CONTRACTED TO OTHER ORGANIZATIONS OR PERFORMED OUTSIDE OF THE UNITED STATES. EMPLOYEE DATA IS FROM JANUARY 2003. DATA FOR PHARMACEUTICALS, CHEMICALS, AND WHOLESALE AND RETAIL SALES IS FOR 2001. INDUSTRIES ARE MUTUALLY EXCLUSIVE, BUT NOT ALL INDUSTRIES ARE SHOWN. SOURCE: NATIONAL SCIENCE FOUNDATION

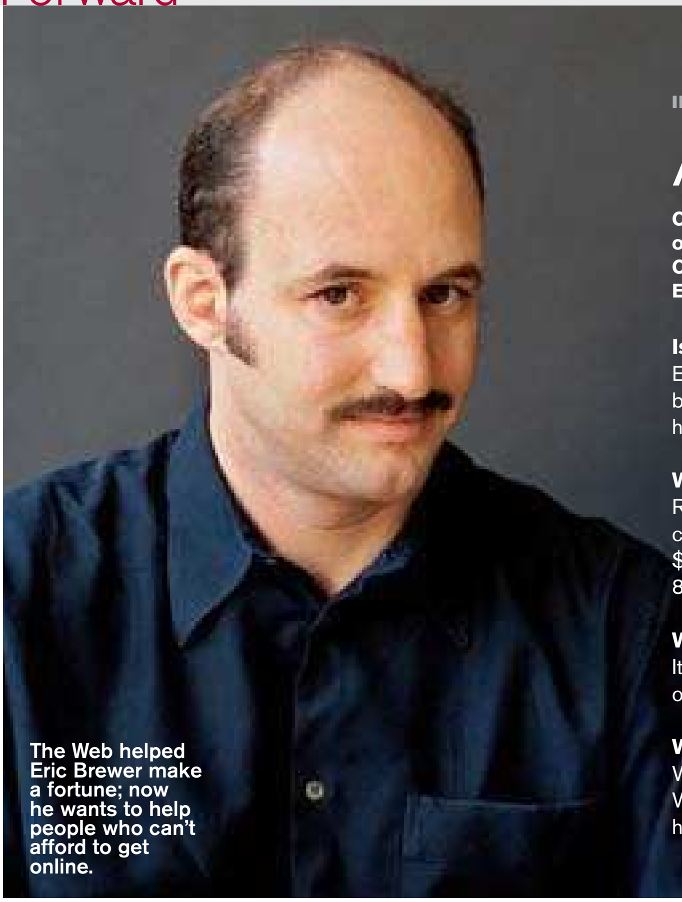
Prototype continued from p. 23

crystal displays that are built into the keys of a PC keyboard. Each screen displays an icon that indicates the function of its key for whatever program is running. The system can also sense what users are doing within a program, anticipate which functions they might need next, and assign those functions to handy keys. Similar keyboard displays exist but are now limited to industrial applications, like cash registers, because of their high cost. United Keys says that by making its technology more compatible with PC keyboard industry standards, it can cut costs by more than half and broaden the technology's reach. The firm says enhanced keyboards could be available this year.

Supersecret Search

The Web isn't as anonymous as you might think: website operators, Internet providers, and hackers can track your activities if they really want to. So for those who want to search medical, legal, and other potentially sensitive sites but don't want anybody to know what they're looking for, computer researchers at Ben-Gurion University of the Negev, in Beer Sheva, Israel, have developed a new search system. When a user conducts a search on a medical site, for instance, the system generates extra, decoy queries—requests for information about other ailments, say—to mask the user's true interests. That may sound suspiciously like Internet saboteurs' methods for flooding websites. "Yes, it does generate more traffic," says Yuval Elovici, who created the system with Bracha Shapira, "but with no malicious intent. That is the price you pay for privacy." Elovici and Shapira are currently using the U.S. Patent and Trademark Office website to test their system, which could be available for public use later this year.

COURTESY OF TOM KEEGAN/WHIPSAW (KEYBOARD); KAI VERMEHR/EBOY.COM (ADVERTISERS)



The Web helped Eric Brewer make a fortune; now he wants to help people who can't afford to get online.

INTERNET

All-Access Digital

Cheap computing still isn't cheap enough, says Eric Brewer, founder of Web-search company Inktomi. Brewer heads the University of California, Berkeley–based Technology and Infrastructure for Emerging Regions project.

Is Moore's Law letting us down?
Even a hundred-dollar computer is too much for billions of people. The bigger problem is that we design technologies for the First World, then hand them down and hope they're useful. A lot of times they're not.

What's your focus?
Reliable shared infrastructure and low-cost, point-to-point wireless connections. We've already got 10-kilometer broadband links, using $800 worth of modified Wi-Fi gear. Simulations say we can get to 80 kilometers.

Who runs it?
It has to be local stakeholders on the ground. They can be volunteers or entrepreneurs.

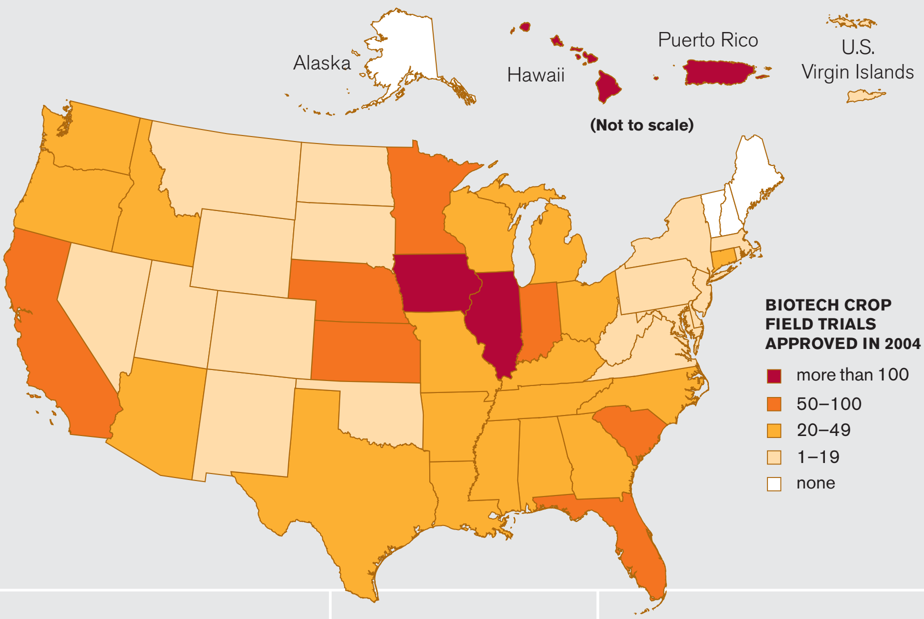
Why not just invent another great search engine?
When you have a billion dollars—even just on paper—you start to think, What do I do with this stuff? I don't have all the money anymore, but I still have the interest in getting the benefits of IT to everyone. Spencer Reiss

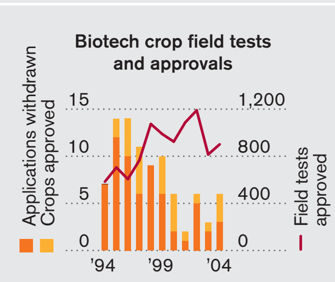
PHOTOGRAPH: TIMOTHY ARCHIBALD

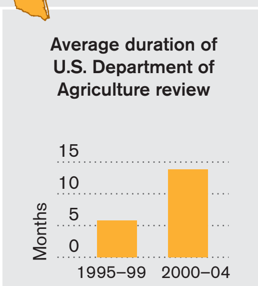
BIOTECH

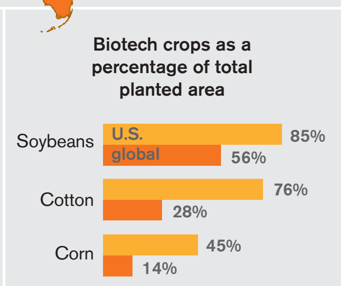
U.S. Agricultural Innovation Withers

The number of U.S. field trials of genetically modified crops has climbed since the mid-1990s. But the number of new biotech crops *approved* by the U.S. Department of Agriculture has declined in the same period, and many of the crops being submitted for review have the same traits as existing products, according to a recent report by the nonprofit Center for Science in the Public Interest. What's more, regulatory review times have doubled, exacerbating the dearth of novel submissions.









SOURCES: INFORMATION SYSTEMS FOR BIOTECHNOLOGY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, U.S. DEPARTMENT OF AGRICULTURE, INTERNATIONAL SERVICE FOR THE ACQUISITION OF AGRI-BIOTECH APPLICATIONS

STARTUP

Deciphering DNA, Top Speed

Helicos BioSciences aims to expedite sequencing, enable genomic medicine

THE SEQUENCING OF the human genome is one of biotech's greatest technical achievements to date. But some biomedical researchers argue that they won't truly understand how genes contribute to health and disease—and so won't be able to turn genomic knowledge into new cures and treatments—until they can compare, letter by letter, the DNA sequences of thousands of sick and healthy people. And that is just not possible with today's technology; using about 100 state-of-the-art sequencing machines to fully sequence the 3.2 billion DNA letters that make up one person's genome would take six months and cost $20 million to $30 million.

A few companies, however, are close to commercializing technologies that could begin to chip away at the high cost of decoding genomes. Among them is one-year-old startup Helicos BioSciences, located in Cambridge, MA. Using technology developed by Stephen Quake, a Stanford University biophysicist, and with $27 million in venture capital funding, Helicos is currently building its first sequencing machine. The company intends to place the device in an academic lab for testing by the end of the year. Helicos's first commercial sequencing machines will be ready for sale by the end of 2006 or early 2007, says president and CEO Stan Lapidus.

COMPANY: Helicos BioSciences
HEADQUARTERS: Cambridge, MA
AMOUNT INVESTED: $27 million
LEAD INVESTOR: Flagship Ventures
KEY FOUNDERS: Stephen Quake, Stanford University; Noubar Afeyan, Flagship Ventures; Stan Lapidus
TECHNOLOGY: High-speed, low-cost DNA sequencing

Helicos's technology eliminates many of the expensive and time-consuming steps that are central to conventional DNA sequencing. The machine works, in essence, by photographing the process of DNA replication.

Technicians chop up the DNA to be sequenced into short pieces just a few hundred letters long and split each piece into single strands, which will serve as templates for new DNA copies. They take about 1.2 billion of those templates and chemically anchor them side by side, like tiny bristles, on a glass slide. The Helicos machine then washes the slide with DNA-synthesizing enzymes and fluorescently tagged versions of the DNA bases—the molecular building blocks represented by the familiar DNA letters. It introduces copies of just one base at a time; wherever a template strand calls for that letter in the next open position, the enzymes incorporate it into the growing DNA copy. The machine then washes out the extra, unincorporated bases and takes a picture that reveals the newly incorporated bases as dots of lights. Once it has captured an image, the device pumps in chemicals that stop the new bases from glowing, in preparation for another cycle of washes and photos.

The Helicos machine repeats the whole process over and over, building up

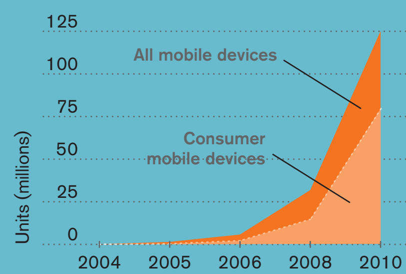
ILLUSTRATION: SHONAGH RAE

ELECTRONICS

Micro Fuel Cells Go Big

December marked the first commercial launch of a micro fuel cell–powered device: a handheld RFID tag reader. Technological, marketing, and regulatory hurdles have made it tough to bring these longer-lasting battery replacements to market. Still, says Frost and Sullivan, micro fuel cells could begin to power laptops and PDAs in 2007. By 2010, shipments of fuel cell–equipped mobile devices could exceed 120 million.

Micro fuel cell–equipped mobile-device shipment forecast



SOURCE: FROST AND SULLIVAN

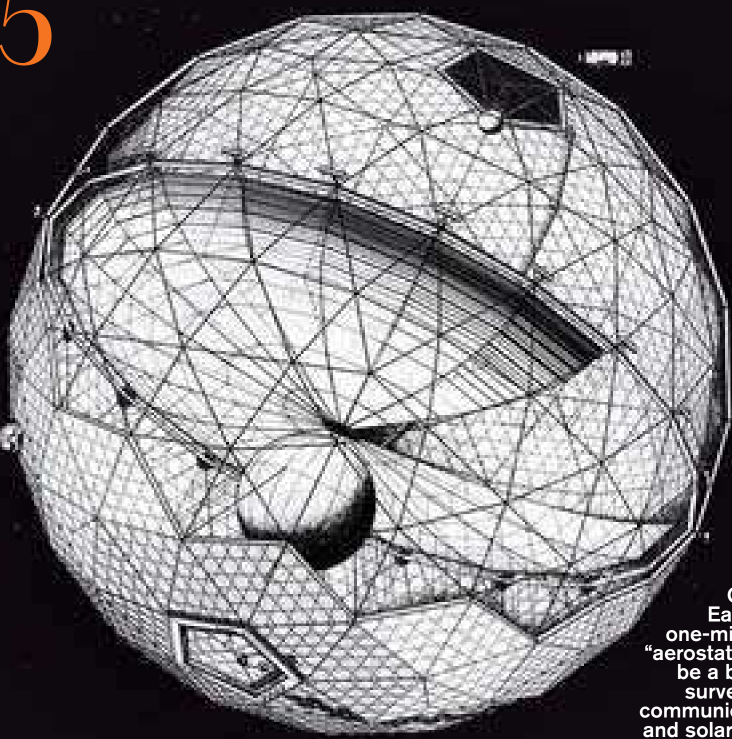
the new DNA copies one letter at a time. A computer analyzes all the captured images to determine the sequence of each short strand; then, using the published human genome sequence as a guide, it pieces all the short sequences together into a single complete one. When Helicos's commercial machine is released, says Lapidus, it will sequence a whole genome start to finish in three days and for a cost of $5,000.

Helicos's basic approach to sequencing, called "sequencing by synthesis," is not unique. But what makes the company's system different from others under development is that it doesn't require that the sample DNA be copied many thousands of times before sequencing. Skipping the copying step translates into easier preparation of samples and lower costs, says Harvard genetics professor George Church, who consults for Helicos. But, he adds, it's not clear yet just how much those advantages will matter in the end. "It's a benefit," he says. "It's just a matter of how big."

Some researchers argue that they won't be able to turn genomic information into new medicines until they can sequence thousands of people's DNA.

And while the magnitude of Helicos's technical advantage remains unclear, what is certain is that the company will have to play catch-up on the path to commercialization. Two other companies—454 Life Sciences, based in Branford, CT, and Solexa, based in Essex, England—each have at least four more years' experience in developing low-cost sequencing. Both 454 and Solexa are gearing up to market their first commercial units this year. "Speed to market is very important in this area," says Tony Smith, Solexa's vice president and chief scientific officer. Helicos will have to figure out the most efficient way of building its machines and proving the technology's value to customers. And by the time the startup does get its machines out the door, it will likely face a tough fight with the more established companies for its share of what's shaping up to be an important and competitive market. Corie Lok

25 years ago in *Technology Review*



Orbiting Earth, this one-mile-wide "aerostat" would be a base for surveillance, communications, and solar energy generation.

Can Space Profits Save the Space Program?

This year is a critical year—and the 1980s a critical decade—for the future of the U.S. in space. With the flight of the Space Shuttle will come the moment of decision: we must then move decisively to open the new window it will provide to economic and intellectual progress.

That coming necessity should be more obvious than it is, say Gilbert W. Keyes and John T. Bosma of Boeing Aerospace Co. "From a viewpoint of technical and financial risk," they told the American Association for the Advancement of Science last winter, "space ventures rate well below industries such as offshore oil, and, to a certain extent, electronics."

"Space is a surprisingly ordinary economic environment," they said. And they think that fact will become obvious when the shuttle begins regular flights sometime in the 1980s.

But most of the plans for space do not sound ordinary at all....[An] example, from... the Franklin Institute's Research Center: a solar-powered sphere *one mile* in diameter to be placed in the stratosphere at an altitude of 30 kilometers as a base for surveillance, research communications, and solar energy generation....

The obstacles to...commercial exploitation of space are financial, organizational, and political—but not technological, [Keyes and Bosma] said. What's needed are "sharp increases" in NASA's budgets for 1980–85 together with tax and other financial incentives "to reduce the risks and costs for industries that participate in fledgling space industries." The goal is to let private industry make space systems self-sustaining so that NASA can concentrate on research....

Without [new appropriations for space science], space may well turn into a military jurisdiction. "We are only beginning to appreciate the full potential of military space systems," Robert A. Davis of Aerospace Corp. told the AAAS. Here, too, the problem is likely to be money. But superimposed on that problem for the military space planner, said Dr. Davis, is the question sharpened by the ever-increasing development time needed for new weapons systems: "How can we be sure that new technology can be introduced at a pace commensurate with its need as well as its availability?"

John. I. Mattill
(May 1980, p. 80)

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HELPING BUSINESS THRIVE ON TECHNOLOGY CHANGE

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Emerging Energy Technologies

HYDROGEN FUEL CELL technology is attracting both scientific interest and government and corporate funding. According to one optimistic scenario presented in a report by the National Academy of Engineering, by 2038, cars powered by hydrogen fuel cells could completely dominate new-car sales, causing automotive gasoline consumption to dry up by around 2050. Meanwhile, sales of hybrid cars, which use a combination of electricity and gasoline, won't reach their U.S. peak until 2024.

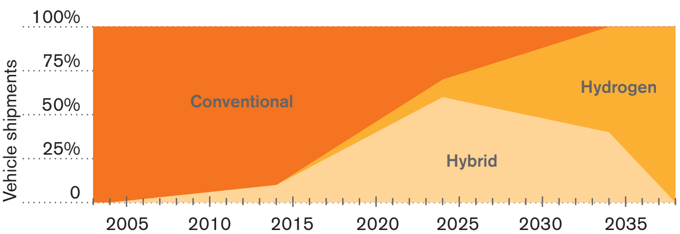
Renewable energy now accounts for about 8 percent of global energy consumption, a figure that's not expected to shift substantially over the next 20 years. Hydroelectric plants are responsible for the vast majority of the renewable power generated in the United States, but their output is expected to increase only slightly over the next 20 years. Wind and biomass generation, on the other hand, should produce an increasing share of the country's renewable energy.

Renewable energy sources continue to draw little interest from venture capitalists. Investment in clean energy technologies hovers around 2.5 percent of total VC spending.

STACY LAWRENCE

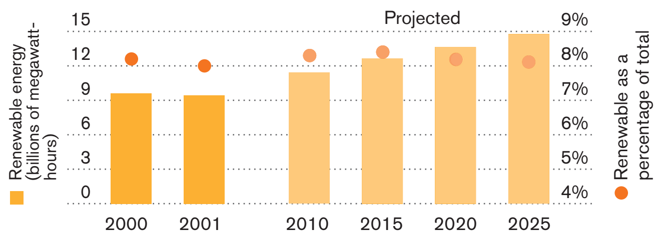
The future of hydrogen

One optimistic projection from the National Academy of Engineering shows hydrogen vehicles constituting all new vehicle shipments by 2038.



Global consumption of renewables stays flat

Renewables are expected to provide a relatively stable proportion of the world energy supply, hovering at around 8 percent.



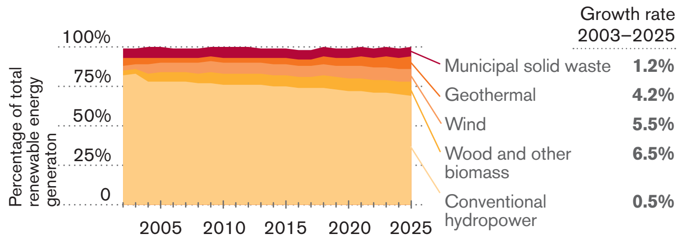
Fueling federal innovation

Much of the federal investment in alternative energies and conservation efforts is made through the Energy Department's Office of Energy Efficiency and Renewable Energy. (Numbers in millions.)

	FY 2005 appropriations	FY 2006 request to Congress	Percent change from 2005
Energy efficiency and renewable energy			
Hydrogen technology	$94.0	$99.1	5.4%
Solar energy	$85.1	$84.0	-1.3%
Energy and renewable-energy administrative and infrastructure	$49.5	$52.2	5.5%
Biomass and biorefinery systems R&D	$80.8	$50.4	-37.7%
Wind energy	$40.8	$44.2	8.4%
Geothermal	$25.3	$23.3	-7.8%
Hydropower	$4.9	$0.5	-89.7%
Energy conservation			
Weatherization and intergovernmental activities	$309.0	$298.2	-3.5%
Vehicle technologies	$165.4	$165.9	0.3%
Program management	$93.0	$89.0	-4.3%
Fuel cell technologies	$74.9	$83.6	11.5%
Building technologies	$65.5	$58.0	-11.5%
Distributed energy resources	$60.4	$56.6	-6.3%
Industrial technologies	$74.8	$56.5	-24.5%
Federal energy management program	$17.9	$17.1	-4.4%
Biomass and biorefinery systems R&D	$7.3	$14.6	200.6%

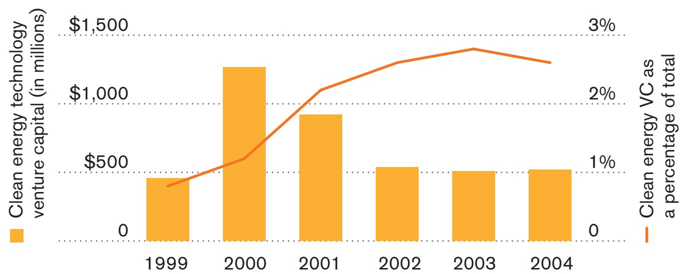
Projected renewable energy generation, by type

Hydroelectric plants provide about 80 percent of U.S. renewable electricity. By 2025, their share is expected to shrink to around 70 percent, as renewables like biomass and wind claim a larger portion.



Venture capital investment

Clean energy technologies have claimed a larger share of VC funding over the last five years, but that share is still only around 2.5 percent.



U.S. DATA ONLY, UNLESS OTHERWISE INDICATED. SOURCES: NATIONAL ACADEMY OF ENGINEERING, NTH POWER, CLEAN EDGE, CLEANTECH VENTURE NETWORK, PRICEWATERHOUSE-COOPERS/NATIONAL VENTURE CAPITAL ASSOCIATION/VENTURE ECONOMICS, U.S. DEPARTMENT OF ENERGY

British Invasion

BAE Systems and WPP Group advance

THE BRITISH ARE COMING! The British are coming! The March 7 announcement that British defense firm BAE Systems would pay $4 billion for Pentagon contractor United Defense Industries tells us two things. First, if there was any question after the invasion of Iraq, there should be no longer: the U.S. and Britain are in this together. The two combined companies will be the sixth-largest supplier to the Pentagon. Second, the acquisition highlights what many growth investors like about mid-tier companies: they are juicy takeover targets. On the day BAE's offer valued UDI at $75 a share, UDI's stock closed at $73.35, 25.9 percent above its previous close.

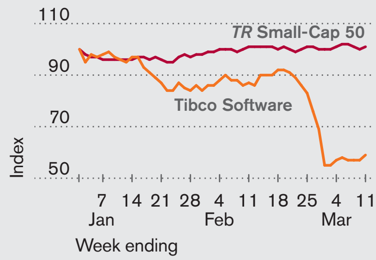
Speaking of Britain and acquisitions, advertising behemoth WPP Group led the list of *TR* 100 gainers in the five weeks ending March 11, climbing 17.8 percent. The company has made a habit of eating competitors whole (Grey Global, Young and Rubicam), and investors bid the stock up in the wake of strong year-end results. These WPP folks must know what they're doing. Or do they? Long-suffering Sony shareholders also enjoyed a boost during the month, as a shaking up of the venerable company—most clearly evidenced by the elevation in March of gaijin Howard Stringer to CEO—continued. A month before, Sony had made another big decision. It dumped WPP subsidiary Y&R from a $100 million account. Duff McDonald

The *TR* Large-Cap 100 and Small-Cap 50 indices live online, where they are updated daily. Visit www.technologyreview.com/trindex.

TR stock index comparison

	% change 2/4–3/11	One-year % change
TR Large-Cap 100	2.5%	9.4%
TR Small-Cap 50	1.1%	18.0%
S&P 500	-0.2%	8.4%

In depth: Tibco Software



After hitting a monthly high in late February, shares of Tibco Software fell for five straight days before the company warned that it would miss its first-quarter numbers. What caused the slide? First, rumors: the sell-off began a week before the Tuesday after-the-bell warning. Then, research: on the day before Tibco's warning, Bear Stearns analyst John DiFucci issued a report predicting missed numbers.

TR Large-Cap 100

	% change 2/4–3/11	Total market cap (millions)
Energy	7.9%	1,309,562
Biotechnology & pharmaceuticals	5.3%	1,169,067
Semiconductors & equipment	4.8%	395,032
Aerospace & defense	3.5%	233,552
Consumer	3.2%	194,152
Telecommunication services	0.3%	795,707
Computers	-0.5%	735,295
Media	-1.7%	479,946
Software & services	-3.8%	507,479
Health care	-3.9%	212,661

TR Small-Cap 50

	% change 2/4–3/11	Total market cap (millions)
Aerospace & defense	24.0%	5,970
Energy	9.5%	15,377
Media	5.9%	12,680
Health care	2.1%	10,218
Telecommunication services	-0.2%	3,595
Computers	-0.4%	18,143
Consumer	-0.5%	3,111
Biotechnology & pharmaceuticals	-5.2%	10,689
Software & services	-6.8%	15,486
Semiconductors & equipment	-6.8%	5,831

TR Large-Cap 100, top gainers

	% change 2/4–3/11	One-year % change
WPP Group (London: WPP)	17.8%	7.8%
Merck (NYSE: MRK)	13.4%	-28.5%
Sanofi-Aventis (NYSE: SNY)	13.4%	12.7%

TR Small-Cap 50, top gainers

	% change 2/4–3/11	One-year % change
United Defense Industries (NYSE: UDI)	43.7%	139.2%
Varco (NYSE: VRC)	28.8%	105.3%
F5 Networks (Nasdaq: FFIV)	20.6%	95.8%

TR Large-Cap 100, top losers

	% change 2/4–3/11	One-year % change
Biomet (Nasdaq: BMET)	-13.7%	5.4%
Boston Scientific (NYSE: BSX)	-12.1%	-27.1%
Viacom (NYSE: VIA.B)	-10.0%	-9.2%

TR Small-Cap 50, top losers

	% change 2/4–3/11	One-year % change
TIBCO Software (Nasdaq: TIBX)	-33.0%	0.5%
Protein Design Labs (Nasdaq: PDLI)	-29.1%	-37.4%
Ciena (Nasdaq: CIEN)	-25.9%	-64.5%

SOURCES: STANDARD AND POOR'S CUSTOM INDEX SERVICES, *TECHNOLOGY REVIEW*

Research in Development

THE CASE: In 2002, IBM bought PricewaterhouseCoopers Consulting. Since then, it has pushed its vaunted research arm to give the same attention to services that it gives to hardware and software. This requires soft research whose benefits are hard to measure. But early results are promising.

Visitors entering the T.J. Watson Research Center in Yorktown Heights, NY, are greeted by glass cases displaying historical calculating machines, from the abacus to Leon Bolle's multiplier. The objects do honor to IBM's history. They also serve as reminders to the people who work here that IBM's products today are not at all what they used to be.

IBM's track record in corporate research is almost unparalleled. The company routinely nabs the greatest number of U.S. patents in a given year. Its researchers have won two Nobel Prizes in physics. Its laboratories invented magnetic storage, the first formalized computer language (Fortran), fractals, the relational database, and the scanning tunneling microscope. If quantum computers ever do arrive, it will be in large part because of developments at IBM Research.

"There is no product in the IBM company that does not start in research, with minor exceptions," says Paul Horn, a solid-state physicist who has run IBM Research since 1996.

But while Horn is proud of IBM's achievements, he believes that the company needs to change the way it thinks about research, for the simple reason that its product mix keeps shifting toward the ethereal. That started with software. Once seen as a mere hardware accessory, software grew in importance after the 1956 consent decree between IBM and the U.S. government, which created the market for packaged software. For decades thereafter, IBM sold more software than any other company (in 2004, its software sales totaled $15 billion, about 16 percent of its revenues). But although software can't be taken apart on a lab bench, the role that R&D can play in its development has always been clear to researchers at IBM. Computer languages, the relational database, middleware, security software—they all met obvious operational needs. But IBM's most recent category of product—services—has more than a few of its engineers scratching their heads.

Speaking about IBM Research, Horn says, "If we were to disappear, there'd be a sudden stop in our products side. I can't make that statement about services."

PricewaterhouseCoopers CEO Samuel DiPiazza Jr. (left) and IBM CEO Sam Palmisano, 2002.

IBM

Headquarters: Armonk, NY
Employees: 319,000
2004 revenues: $96.5 billion

But what, exactly, are services? Within IBM, the word is used in two ways. First, "services" is one of the company's three broad product categories (the other two being physical products and software). Most pure services are sold by IBM's 180,000 consultants and range from wholesale IT outsourcing to training, human-capital management, and the On Demand Innovation Services effort, a broad (that is, vague) effort to make widely disparate systems communicate more effectively, and in real time. These services don't have profit margins as high as those of IBM's proprietary hardware and software, but service sales often follow product sales (and sometimes drive more product sales).

The term "services" is also used by people at IBM to mean any work that helps improve a product or a process. The product could be a piece of hardware or software; the process could be the way consultants present data to clients. But whether services are thought of as discrete products or product enhancers, IBM sees them as critical to its future.

Research at a Crossroads

Horn and the rest of IBM Research find themselves in the midst of a somewhat awkward transition. While products that the company makes have, as a whole, moved across the hardware-software-services continuum, the research that underlies them hasn't quite kept pace. Thus IBM Research appears, in certain instances, as if it's attempting to answer the wrong questions.

Its Zürich laboratory, for instance, is close to completing work on Millipede, a nanomechanical device that can store data at a density 20 times higher than that of magnetic storage. But if Millipede proves commercially viable, it probably won't be built by IBM, because IBM sold its storage division in 2002 as part of an effort to shed low-margin businesses. This February, it sold its once vaunted personal-computer business for the same reason. At the time of the sale, services already constituted slightly less than half of IBM's $96 billion in annual revenues. Now that the hefty—$12 billion—but often unprofitable PC business is gone, services will likely check in at closer to two-thirds of revenues.

COURTESY OF IBM

Horn's challenge, then, has been to take a $6 billion research organization dedicated to work that advances technology products and get it to do work that benefits service businesses. IBM is thus in the process of answering an important question for all technology companies: can corporations perform useful research in the services arena?

At the very least, say many observers, they'll have to try. Roland Rust is a sometime consultant to IBM and director of the Center for Excellence in Service at the University of Maryland's Robert H. Smith School of Business, which is partnered with the company. "It's a no-brainer," Rust says, that as the economy in general shifts away from goods, companies will need to pursue services research. He notes that even General Electric, an industrial giant, now thinks of itself as a services company. And he believes that IBM's approach to services research will ripple through the rest of the industrial world, both because it has a highly regarded research lab and because it has made the hard transition from being primarily a goods company to being primarily a services company.

Henry Chesbrough, executive director of the Center for Open Innovation at the University of California, Berkeley's Haas School of Business, is also unsurprised that IBM is shaking things up. He contends that the academic field of computer science exists in part thanks to IBM's insistence that it wasn't something that belonged to the physics, engineering, or mathematics departments. Chesbrough thinks IBM may help services in the same way, by putting its corporate stamp on the idea that services research should involve operations, marketing, and supply chain management. "Left to our own devices, we'll remain in our silos," Chesbrough says. "I'm excited about it because they're taking a fresh look at a very old problem, and they're among the very first to do something about it."

But being among the first to do something is not necessarily the same as doing it quickly. "There was always a feeling we had to do something in services, as soon as we'd had a services business," Horn explains. But the company had problems determining just what it should do. IBM Research had pursued formal studies of services projects, and it had even developed corporate strategies, such as the autonomic-computing initiative Horn unveiled in 2001, that involved elements of the service business. But these projects were geared toward physical products, not service products.

Then everything changed. IBM's tentative approach to supporting services ended in July 2002, when it announced that it was planning to buy PricewaterhouseCoopers Consulting. By the end of 2003, the two companies' first full year of merged operation, close to half of IBM's revenues were coming from services. In contrast, services accounted for less than 15 percent of R&D spending. "So did that mean Lou [Gerstner, then the CEO] could say, 'Do I need only half the R&D spending?'" Horn recalls wondering. "Those things get you thinking."

"Services Is a People Business"

Horn wasn't the only one thinking. In May 2002, Paul Maglio, a cognitive scientist in IBM's Almaden research lab in San Jose, CA, also had change on his mind. Maglio was working on user-interface research, and over Mai Tais with friends at a Web conference in Hawaii, he spun out a scenario he'd been working on with IBM colleague Rob Barrett, in which the company looked at technology research differently. "Services is a people business," Maglio says now. "I'm a cognitive scientist; I'm interested in people generally. What we were doing [in human-computer interfaces] was fine, but it didn't get the whole picture. I thought we could create a new breed of research."

In particular, Maglio thought that IBM simply didn't know what its customers actually did with technology. He also didn't think anyone knew whether IBM's consultants understood what its customers wanted. He thought there was a need for a broad study that drew on what he called the "human sciences."

Maglio and Barrett were proposing work that would be much different from what IBM, with its roots in hard science, was used to doing. But they found a willing ear, and a champion, in Jim Spohrer, then the chief technology officer of IBM's venture capital unit. After a series of discussions starting in July 2002, around the time IBM announced the PricewaterhouseCoopers deal, Spohrer agreed to take the idea first to Robert Morris, head of the Almaden research lab, and ultimately to Horn. He nixed the human-sciences part of the pitch; instead, he proposed using the new approach to help Horn solve his biggest problem: determining how to help the services business. When Spohrer brought the idea to Horn, he described services as a "human business that needed human research."

The timing was excellent. Horn was already interested in seeing the company develop the ability to do softer research. "What we were doing in services was very much on the quantitative side, and I thought we needed a break from it. We hadn't done anything at all on how technology affects people," Horn says. His push to support services thus converged with Maglio's push to make research more human. That convergence meant not only that services would become an important subject of research, but also that hardware and software research would begin to include some "soft" work. This marked a turning point for IBM—and a good one, Spohrer contends: "Research reinvents itself every 10 years. So it was a good thing to do."

That December, Horn signed off on the idea. Spohrer was tapped to direct services research at Almaden. His first outside hire was a business anthropologist, Jeanette Blomberg. He wanted her to study work practices, including how

So far, it may be that the mathematics arm of IBM Research has done the most work on services. Part of the group's charge is to devise algorithms to improve the way businesses use information technology.

technology users collaborate. Meanwhile, Maglio began to investigate what systems administrators actually do. He found that they spent between 60 and 90 percent of their time communicating with other systems administrators about systems issues. Armed with that knowledge, IBM began developing tools to help systems administrators write and share "scripts"—the short, simple programs they use to coördinate the work of other programs.

So far, it may be that the mathematics arm of IBM Research has done the most work on services. Part of the group's charge is to devise algorithms to improve how businesses use information technology. Brenda Dietrich, manager of the mathematical-sciences research department at the Watson Research Center, says her 90-person unit sees great potential in even the softest research being done on services. "What Jim's group is doing is a good source of data for my models," which are currently too simplistic to reflect the real world, she says. Dietrich believes that if IBM can get better data on what people actually do with technology, her group can produce more-useful algorithms. "If we can really get the data [Spohrer is] talking about, that's powerful."

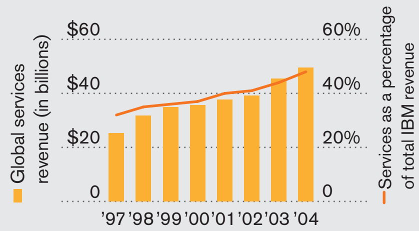
About half of those 90 researchers are now engaged in services work at any one time, either traveling with consultants or working on projects that will help consultants. Dietrich says that IBM's expectations for its research arm have changed gradually but dramatically in the 20 years she has worked there. "It used to be that you got asked, 'Have you got anything into products?'" she says. But an analogous question about services is harder to answer. Development work on services tends to wind up as part of a process, not a product. Discrete product features are easy to point to; the parts of a process are broader, and mushier.

Does All This Work Increase Profitability?

Two and a half years after starting to pursue services science, IBM can point to some successes. The company has a fixed procedure for measuring what it calls "accomplishments," and Horn estimates that about 15 percent of the accomplishments by research now involve services. Research has had 250 direct consulting engagements since 2002. And in the fourth quarter of 2004, it spawned two new practice areas, WebFountain and the Center for Business Optimization.

Services Revenue

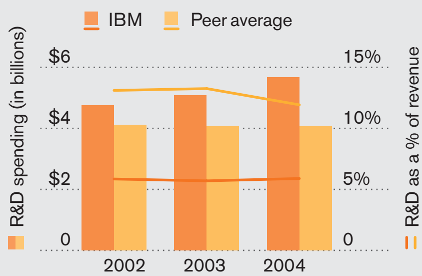
Services revenues have grown to constitute almost half of IBM's total revenue, from less than a third in 1997.



SOURCE: REVERE DATA

R&D Spending

IBM spends more money on technology research and development than its peers but a far smaller proportion of its revenue.



PEER AVERAGE IS BASED ON THE 10 R&D TECHNOLOGY COMPANIES WITH THE HIGHEST R&D SPENDING LISTED ON U.S. PUBLIC MARKETS. SOURCE: REVERE DATA

Both are fledgling but promising. WebFountain is a set of processes for organizing and analyzing huge sets of disparate data. A WebFountain application might involve surveying text on the Web and deducing what people are actually saying, rather than just returning instances of keywords. That work is of obvious interest to IBM customers that have, say, customer service departments that need to gauge complaints or answer questions.

The Center for Business Optimization helps clients tighten up operations. It recently created what it calls a Pharmaceutical Production Refactoring Tool, which helps large drugmakers reduce the risk of having to shut down manufacturing facilities because of failed health inspections. This tool could prove especially useful now, in light of recent changes in drug-manufacturing regulations, which mean that if the U.S. Food and Drug Administration finds a problem with a single production line at a manufacturing facility, it will shut down the entire site until the problem is resolved. Thus, "something low-margin can wipe out your entire facility revenue," notes Krishna Nathan, head of IBM's Zürich Research Lab and vice president of services research. "It's a huge problem for the industry. [Drug manufacturers] need to refactor the risk and restructure it across all their sites."

To create a product that would help meet that need, IBM researchers in November 2004 worked with IBM's Business Consulting Services unit to devise algorithms that would quantify the risk of failure presented at each site and suggest changes, based on historical data from drugmakers. According to Nathan, in a pilot case involving one drugmaker, initial tests showed that the IBM tool had the potential to reduce risk by 30 percent.

The push now is to do more, faster. No one at IBM Research thinks the division is getting enough done on the services side. Over the past year, IBM has started referring to its research work as "services science," but there are people even in the services group who can't say those words with a straight face. Nathan added "services" to his title only in September, when Horn decided he wanted the research department to accelerate its services efforts.

"We're making a lot of progress, but would I like it to be faster? Yeah, I would," says Horn. He hopes that in five years, half of IBM Research's "accomplishments" will come from its work on services. But he thinks it may take years for the department to become as services oriented as he thinks it must be to best serve IBM's needs.

Services have clearly been good business for IBM. Less clear is whether services research is good business; it's too new an area for us to know for sure. But there are encouraging signs: IBM's On Demand Innovation Services program, which basically farms out the talents of the research staff, last year generated more than $300 million in revenues. That might seem an insignificant portion of a $46 billion service business. But it more than triples the revenues from the year before. Growth like that is hard to ignore—and could be a sign of more to come.

MICHAEL FITZGERALD

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Starting Up, Post-Bubble

THE CASE: The two engineers who created price-comparison site mySimon were among the lucky entrepreneurs who struck it rich before the crash. Now they think they can beat Google and others in online product information and shopping. But the rules for building a startup have changed.

TOO MUCH INFORMATION. In conversation, it means roughly "Stop! I didn't want to know that." But it's also a cry heard more and more often from search-engine users who type in a generic query like *digital cameras* and get back an Everest of results (21 million at Google, 21.5 million at MSN Search, and 38.1 million at Yahoo, to be precise). For shoppers in pursuit of product reviews or retail listings, general-purpose search engines just aren't the right tools.

But shopping portals like Shopzilla, PriceGrabber, Shopping.com, and Froogle have their own shortcomings, argues Silicon Valley entrepreneur Michael Yang. They generally assume that shoppers have already decided what they want to buy and are simply comparing prices. "But shopping is really a two-stage process," says Yang, who is 43. "Once you decide what is the best product, *then* you start comparing prices. And the comparison-shopping sites are only focused on getting you the best price."

Yang should know. Along with fellow Korean-born engineer Yeogirl Yun, he launched price comparison site mySimon in 1998. MySimon was one of the earliest and most successful online shopping aids, attracting millions of users and $30 million in venture capital in its first 18 months. In early 2000, CNET acquired mySimon for $700 million, providing a princely return to its investors and allowing its founders to walk away with fortunes in the "double-digit millions," in Yang's words. It was one of the rare examples of dot-com dreams come true.

Michael Yang (left) and Yeogirl Yun are going shopping again.

JOHN SOARES

Become.com

Headquarters: Mountain View, CA
Venture funding raised: $4.5 million
Employees: 24

But Yang and Yun weren't sated by the experience. After spending a few years on other projects, the two are back together and taking a second run at the online-shopping market. This time they're building a new type of search engine that focuses exclusively on product-related information. And that might be just the beginning: the engine itself, they say, uses fundamentally new search algorithms that could be adapted to any specialized, or "vertical," category. A beta version of Yang and Yun's site, called Become.com, debuted in February.

But can a pair of dot-com millionaires strike gold twice? (Or thrice, in Yun's case: after mySimon, he developed a search engine called Wisenut, built a solid base of users, and sold it to Looksmart.) These days, the odds are unfavorable for *any* startup. Add to that the extreme caution now endemic among Silicon Valley venture capitalists, the surfeit of existing shopping sites, and the fact that Yun and Yang are taking on Google, Yahoo, and Microsoft all at once, and their plan begins to sound brash.

Yang immigrated to the United States with his parents at age 14, earned degrees in electrical engineering and computer science at the University of California, Berkeley, and Columbia, did stints as a chip designer at Xerox and a marketer at Samsung, and got a night-school MBA from Berkeley. Yun graduated from Seoul National University in 1993 with a degree in computer engineering, won a national scholarship in computer science, earned a master's in the subject at Stanford, and went on to found an Internet software startup called One-Oh. By that time, Yang was running video-card maker Jazz Multimedia, and he and Yun first met when Jazz acquired One-Oh. When Jazz itself folded in 1998, the pair decided to start an Internet business together.

They settled on comparison shopping, a habit Yang says he acquired as a high-schooler earning a low wage at Seven-Eleven. "There were a couple of startups that were already doing that, but they weren't doing it very well," Yang says. (One of them, Jango, was absorbed in 1997 by the doomed search portal Excite, and the other, Junglee, was acquired by Amazon.com in 1998.) Their creation, mySimon, was built around a "virtual learning agent" designed by Yun to extract prices, product details, and other relevant data from merchants' online catalogues, each of which was structured differently. "These days we don't need that agent technology, because most merchants package their information in a standardized XML [extensible markup language] structure," Yun says. "But back then no one wanted to give out that information"—so Yun's team became expert at extracting it.

Between April 1998 and December 1999, 10 million users flocked to mySimon, and its staff grew from two to 60. Yang says he and Yun would have stayed on as the company's leaders, but by early 2000 its investors were itching to cash out.

Comparing the Comparison-Shopping Sites

More than 50 million people visited comparison-shopping sites in February, up almost half from the year before. (A multisite visitor counts once toward the total.)

U.S. DATA FOR FEBRUARY 2005. SOURCE: COMSCORE MEDIA METRIX

CNET's offer of $700 million—made just months before the dot-com crash—was impossible to refuse. (MySimon continues to operate today as part of the CNET publishing empire.)

While Yun went on to start Wisenut, Yang started a family. He says the years after mySimon gave him time to think more about what makes a search engine successful—and to watch Google rise to greatness. "I really got excited about challenging Google by developing a new search engine company that could give them a run for their money," Yang says. In early 2003, he started reading papers about PageRank, Google's algorithm for sorting search results, and started looking for partners who could build something better. "One day it just dawned on me—I should recruit Yeogirl."

Yun, who having sold Wisenut was in law school in Korea at the time, was initially cautious about taking on the search giant. "Google is a strong company," Yun says he told Yang. "I advised Michael to think about something else." But when Yang gave a half-hour pitch over lunch that grew into a six-hour brainstorming session, Yun was hooked. It helped, of course, that Yang was promising to put $2 million of his own savings into the venture.

Any search at Become.com will illustrate one of Yun and Yang's first strategic decisions: to grant a high rank in search results to impartial product-review sites such as ConsumerReports.org and ConsumerSearch.com. Those sites appear in part because Become has a human element: a small team of researchers locates authoritative sites and places them into the site's index. Machine-learning software then ranks other pages partly according to their relation to the authoritative sites. That's a big departure from the approach taken by PageRank, which is fully automatic and sorts the pages resulting from a given query mainly according to the number of other pages that link to them. The more incoming links, the assumption goes, the more popular a page, and the more popular, the more relevant. But "with popularity-based link analysis, sites like ConsumerSearch.com would not always appear high in the results," says Yang. "We fundamentally believe that there are certain things that humans can do better than algorithms."

That's not to say Become lacks clever algorithms of its own. For one thing, Yun and his small team of engineers (who were hired only after passing an exhaustive 20-hour programming test) devised a new type of crawler, which is a program that scans the Web and copies pages into a search engine's index. Become's crawler has been trained to recognize and throw out spam pages and non-shopping-related information. Then there's Yun's proudest accomplishment, the site's core algorithm for sorting search results. Called AIR, for affinity index ranking, it differs from Google's PageRank algorithm in two ways. First, when AIR assesses the importance of a given Web page, it takes into account the *topics* of the pages linking to it. (PageRank considers some elements of the context surrounding an incoming link, but not the page's overall topic.) AIR rewards pages that have on-topic incoming links. Second, AIR penalizes pages that have outgoing links to off-topic pages. (PageRank does not examine a page's outgoing links.) AIR's dual process of rewarding and punishing pages based on the primacy of a specific topic means that the top search results for a query like *refrigerators* will be those most closely related to buying a refrigerator, not necessarily those with the most incoming links, as with PageRank.

For now, Become's only revenues come from the keyword-based ads provided to thousands of sites by Google's AdSense program. (Advertisers pay site owners for every click-through.) Later this year, the site will add classic price-comparison pages and charge merchants to list their wares. Become will earn a fee for every click-through to a merchant site, and a commission for any sales resulting from such click-throughs. Meanwhile, Yang says the company has enough capital—$4.5 million, including $2.5 million from one of mySimon's initial backers, Japanese corporate investor Transcosmos—to keep its team of 24 employees running. That's a lot less than the $30 million mySimon accumulated to support its 60 employees, but Yang says that's deliberate. "Before, it was 'Get big fast.' It was land-grab mentality. Now it's 'Get profitable fast.' And there is value in being self-sufficient. You don't have to be at the whims of investors." The company is currently trying to raise $12 million in second-round financing.

Officials at Transcosmos don't take offense at Yang's attitude. "Number one, we are a big fan of the comparison-shopping category," says Shin Nakagura, vice president of business development at Transcosmos's U.S. subsidiary. "Number two, we made a big return on mySimon, so it's relatively easy to get the money together. Number three, we know those guys. And I think Become.com's approach—starting with the more technically difficult point, pure search, and then adding the product comparison service—is a very good idea."

Indeed, the longer one spends with Yang and Yun, the clearer it becomes that Become is a specialized-search company in a shopping site's clothing. It doesn't take much prodding to get Yun to admit that AIR could be applied not just to shopping but to any well-bounded search domain, such as health care—thereby chipping away at the audiences for general-purpose search sites. As Yun says, "I really feel that Become can become anything." But he understands that in today's climate, he won't attract large investments until he proves that his first business can make money. **WADE ROUSH**

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A Breakthrough Isn't Enough

THE CASE: Transmeta, which was to have been a market-grabbing pioneer in low-power microprocessors, is in tatters. Its failure serves as a cautionary tale to companies long on innovation and short on execution.

It wasn't the Intel monopoly that dealt Transmeta, one of the highest-flying chip companies to come out of Silicon Valley, its mortal blow. The wound was self-inflicted. The startup let down its customers, chip buyers for computer makers who had stuck their necks out to get their companies to use Transmeta's unproven but promising low-power processors.

When the Santa Clara, CA, company came out of stealth mode in January 2000, it was swept up on a wave of hype. It had the right technology to pioneer low-power microprocessors, which, because they use less battery power and throw off less heat than other chips, allow laptops to be both speedy and thin. If Transmeta had hit its performance and power targets, it could have taken leadership away from Intel—which had focused mainly on cranking up the megahertz—in the fastest-growing segment of the PC industry. Laptops are now close to half the market.

David Ditzel, one of the designers of Sun Microsystems' first Sparc chip, which helped create the workstation/server market, founded Transmeta in 1995 and raised money from the likes of Paul Allen and George Soros; the company's initial public offering in late 2000 brought in $273 million. The game plan was clear. Transmeta was supposed to break in with laptop chips and then pioneer low-power gadgets of a type that hadn't previously existed, such as one-pound laptops and handhelds that could run Windows. The company could have become profitable with just a fraction of the $27 billion PC microprocessor market, selling chips to the likes of Toshiba, IBM, and Hewlett-Packard. But it made mistakes.

First, it took a long time to design its chips. It was five years before Transmeta announced its first product and almost another year before its first chip shipped. Also, the company wasn't conservative enough in its choice of manufacturer. It bet that Taiwan Semiconductor Manufacturing would be able to roll out an advanced manufacturing process on schedule. But Taiwan Semiconductor faltered, as do many chip makers when implementing new fabrication equipment and materials. This caused a big delay in chip deliveries, a consequent loss of face for customers, and the erosion of Transmeta's lead over Intel.

"It's almost a Greek tragedy," says Nathan Brookwood, an analyst at Insight 64 in Saratoga, CA. "All they needed was the chorus in the back. They promised a tremendous amount and didn't really deliver on those promises."

Transmeta's Efficeon TM8800 may have come too late.

Transmeta

Headquarters: Santa Clara, CA
Stock price, January 2, 2001: $20.69
Stock price, January 3, 2005: $1.58

Problems with execution were magnified by a high-maintenance design. Transmeta had taken the novel step of moving some functions ordinarily performed in hardware into software, which reduced the size of its chip and lowered power consumption; it expected to make up the difference with increased processing speed. But the task of developing and constantly updating the added software proved to be a drain on company resources.

When Transmeta lost its lead in low-power chips, it awoke a sleeping giant in Intel, which launched a low-power Pentium M chip in 2003 and took most of the market with the Centrino, which aggregated everything computer makers needed to build wireless-network laptops.

Then the economy fell into a recession. Transmeta's sales slipped from $35.6 million in 2001 to $17.3 million in 2003. The company tried again with its second-generation chip, the Efficeon, but it never won back customer loyalty, and Intel's momentum grew. The cutting-edge portables where Transmeta dominated never became a high-volume market.

Transmeta has been up for sale for at least five months. But with a market capitalization of around $200 million, it has no takers at present. Advanced Micro Devices, the number-two PC microprocessor maker behind Intel, could use Transmeta's technology but hasn't been willing to pay the steep price. And while Intel could have used Transmeta's technology five years ago, it doesn't need it now.

The company's last resort is to license its LongRun2 technology, which saves power by reducing the "leakage" of electrical current across transistors that are supposed to be turned off. NEC, Fujitsu, and Sony have licensed LongRun2. But the revenues that have resulted—a few million dollars a quarter—won't solve Transmeta's problems. The company has told its customers that they can license its chip designs, but that it will fill orders only for existing chips. At press time, Transmeta had only $53 million in cash and had been burning through $25 million a quarter.

"This is the way Silicon Valley works," says Paul Saffo, research director for the Institute for the Future in Palo Alto, CA. "Companies make mistakes, and we learn from failure, not successes. Innovation doesn't always win." ■

COURTESY OF TRANSMETA

Whither the Renaissance Man?

We need to save the diversity of the individual.

Michael Hawley held the Alexander W. Dreyfoos Professorship at the Media Lab at MIT, where he was also director of special projects. He has worked on a wide array of creative applications of technology and led students on numerous global expeditions.

Our current age of information has rightly been called a second renaissance. But what ignites a renaissance? It has to do with bringing together ideas and cultures in fresh ways and with unprecedented intensity. That's the reason Gutenberg was so important to the first renaissance: the printing press, the new technologies that enabled its invention, and a burgeoning shipping trade were the Internet of their day. Ideas began to move en masse and with a momentum that was unimaginable before. Thanks to the facility of Western European character sets, printing with movable type took off in Europe, helping spark an economic boom that left much of the rest of the world struggling to catch up.

The digital-media revolution enabled our current renaissance. From Ethernet to Internet to World Wide Web to Google, from silicon biology to nanoscience, worlds of ideas have collided. Just as a 16th-century Renaissance man felt empowered by a bundle of books in his saddlebag, a 21st-century renaissance woman with a laptop feels she has the entire store of human knowledge at her fingertips.

The irony of our renaissance, though, is that renaissance men and women are in short supply. Such an intense global mix of cultures, ideas, and innovations, all apparently a mouse click away, would seem to demand broad educational perspectives. Yet most schools persist in turning out laser-focused young professionals. To make a dent in a particular field, a person has to devote a good chunk of his or her lifetime just to getting to the starting line. This doesn't favor the jack-of-all-trades.

The four years of an undergraduate education (for the minority of the population that gets that far) have become less of an exploration and more of a routine. Even the path to college has become a pipeline of preparatory crash courses, tests, interviews, and campus visits. Graduate schools are even more constricting. In an age that is fomenting the greatest expansion of knowledge—and of its means of distribution—in history, our educational system is churning out ever more narrowly focused scholars. One wonders if, along with biodiversity and cultural diversity, the diversity of the individual mind might be another casualty of modern life.

I'm a big fan of Ben Franklin. The son of a poor soap maker, Franklin loved to read and apprenticed in a print shop when he was 12. By the ripe age of 24, he had settled in Philadelphia and bootstrapped his own printing business. He taught himself French, Italian, and Spanish. He bought a newspaper, the Pennsylvania *Gazette*, and turned it into one of the most successful papers in the colonies. He organized Junto (a working man's group devoted to individual and community betterment). He founded a fire company, an insurance company, and a hospital. He founded the Library Company of Philadelphia, the nation's first subscription library, and the American Philosophical Society.

In his 40s, Franklin retired from his prosperous franchises and got into technology. By then he had already invented the heat-efficient Franklin stove, and swim fins. He also invented the glass armonica. His most celebrated scientific work, of course, was his study of lightning and electricity. Later in life, as his eyesight worsened, he invented bifocals. In the political and diplomatic arena, Franklin worked for independence with Jefferson, helping to draft the Declaration of Independence.

He died at age 84, having just published an antislavery treatise. His was an awe-inspiring life, but I am especially fond of one of the young Franklin's self-improvement exercises. He had identified 13 moral virtues—waste nothing; avoid trifling conversation; practice moderation; aspire to justice, cleanliness, and tranquility; and so on—and kept a scorecard on which he graded himself on how well he realized them. Benjamin Franklin simply wanted to be a better person and to lead a better life.

Nobody said getting your face on money was easy. In today's complex world, perhaps it's simply not possible for someone to lead a creative life that contributes so seminally and so powerfully across so many areas.

Yet we need to be concerned with our intellectual ecology. Global computer-mediated communication presents a new kind of leveling force. But will the enriched pool of online knowledge promote more specialization, or will it promote more sharing among fields? The answer is up for grabs. In that case, how should we prepare ourselves for constructive, inventive lives? My best answer had always been, continually invest in knowledge that won't wear out. But then I found an even better tip for lifelong learning, thanks to Ben Franklin: when you're finished changing, you're finished. ■

PHILLIP MOWERY

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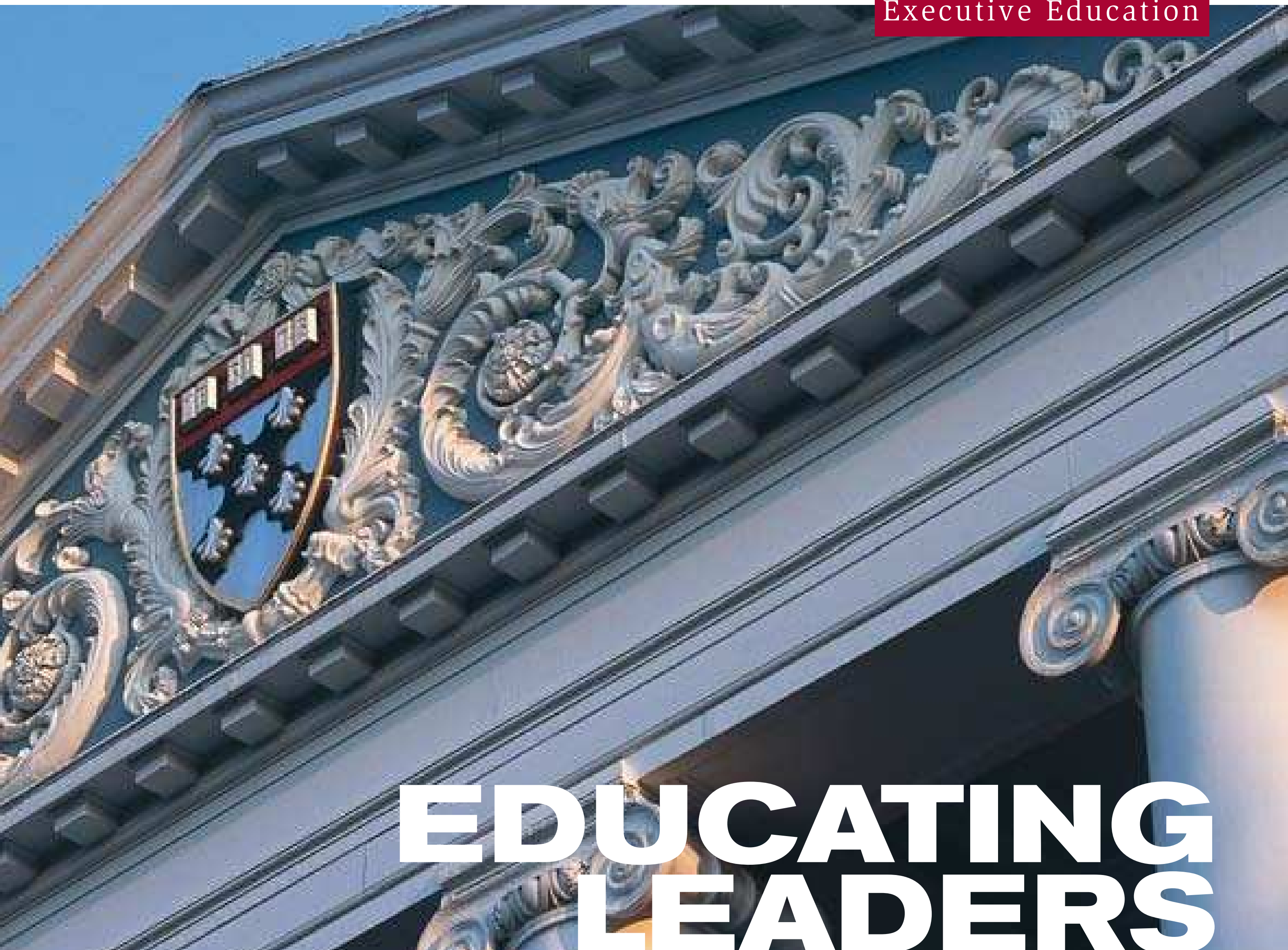

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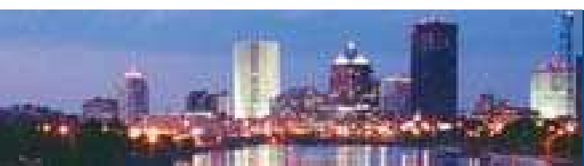

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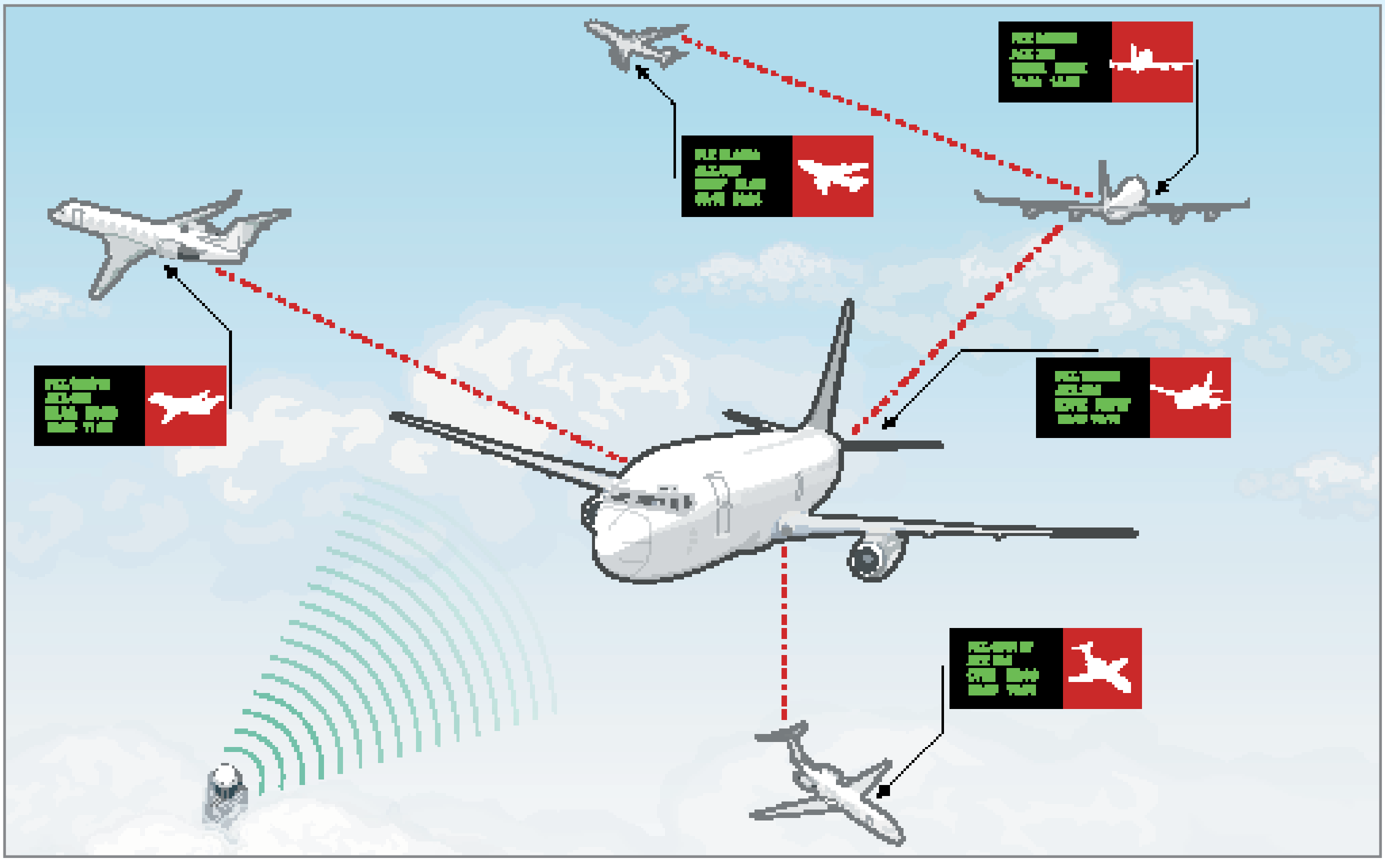


AIRBORNE NETWORKS ILLUSTRATION BY +ISM

Airborne Networks

AVIATION An Internet in the sky could let planes fly safely without ground controllers. By David Talbot

The technology that underpins the air traffic control system hasn't changed much in a half-century. Planes still depend on elaborate ground-based radar systems, plus thousands of people who watch blips on screens and issue verbal instructions, for takeoffs, landings, and course changes. The system is expensive, hard to scale up, and prone to delays when storms strike.

An entirely different approach is possible. Each plane could continually transmit its identity, precise location, speed, and heading to other planes in the sky via an airborne network. Software would then take over, coördinating the system by issuing instructions to pilots on how to stay separated, optimize routes, avoid bad weather, and execute precise landings in poor visibility.

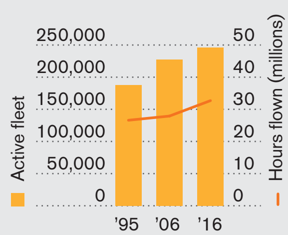
In the near term, such technology could save travelers time and might reduce fuel consumption. Long term, it could revolutionize air travel by enabling more planes to fill the sky without the addition of infrastructure and staff. Vastly greater numbers of small planes could zip in and out of thousands of small airfields (there are 5,400 in the U.S. alone), even those with no radar at all. "The biggest holdback to the number of airplanes that can be in the sky is that air traffic controllers are separating aircraft by hand," says Sally Johnson, an aerospace engineer at NASA's Langley Research Center. "Until you get away from that paradigm, we are at the limits of what you can do."

As a practical matter, airborne networks that rely on software and cockpit computers rather than humans to issue instructions are still decades away. But in June, NASA plans to demonstrate a prototype of such an automated system at a small airport in Danville, VA. A computer at a ground station near the airport will receive data from multiple planes and give the pilots their initial holding fixes, then tell them what planes they're following and where to go if they miss their approaches. In the planes, cockpit displays will show pilots where the other planes are, and a computer will give them instructions that guide their trajectories.

Future systems might go further: planes would communicate not just via a computer on the ground (or via satellite) but directly with each other, relaying information from other planes in an Internet-like fashion. This radical advance in airborne networking could come from research funded by the Pentagon—the midwife of today's terrestrial Internet. The vision is that not only navigational data but information about targets, real-time intelligence, and bombing results would flow freely among manned and unmanned military planes, to vehicles on the ground, and up and down chains

General Aviation Forecast

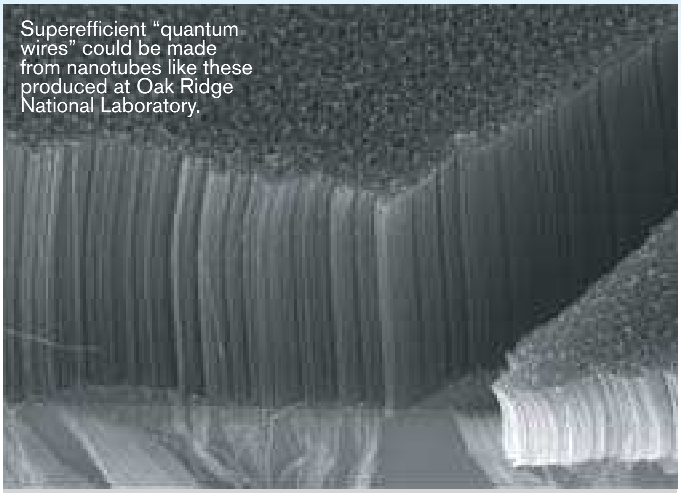
America's skies will grow ever more crowded in the coming decade, as the number of small aircraft multiplies.



SOURCE: FEDERAL AVIATION ADMINISTRATION

of command. “There is a terrestrial backbone of hardwired connections, and there will be a space backbone between satellites. What we are talking about adding, for aircraft, is an equivalent third backbone in the sky,” says Dave Kenyon, division chief of the Technical Architectures Division at the U.S. Air Force Electronic Systems Center in Bedford, MA.

The U.S. Air Force is beginning to define the architecture of an airborne network and hopes to begin actively developing and testing the network itself between 2008 and 2012, Kenyon says. Taken together, the military research and the related air traffic control research into airborne communications networks could change how we travel in the decades to come.



Superefficient “quantum wires” could be made from nanotubes like these produced at Oak Ridge National Laboratory.

Quantum Wires

POWER TRANSMISSION Wires spun from carbon nanotubes could carry electricity farther and more efficiently. By Erika Jonietz

Richard Smalley toys with a clear plastic tube that holds a thin, dark gray fiber. About 15 centimeters long, the fiber comprises billions of carbon nanotubes, and according to the Rice University chemist, it represents the first step toward a new type of wire that could transform the electrical power grid.

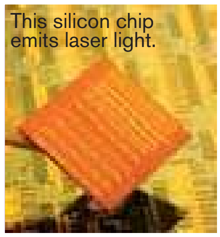
Smalley’s lab has embarked on a four-year project to create a prototype of a nanotube-based “quantum wire.” Cables made from quantum wires should conduct much better than copper. The wires’ lighter weight and greater strength would also allow existing towers to carry fatter cables with a capacity ten times that of the heavy and inefficient steel-reinforced aluminum cables used in today’s aging power grid.

The goal is to make a wire with so little electrical resistance that it does not dissipate electricity as heat. Smalley says quantum wires could perform at least as well as existing superconductors—without the need for expensive cooling equipment. The reason: on the nanometer scale, the weird properties of quantum physics take over, and a wire can carry current without resistance. But until a couple of years ago, no one knew whether this amazing property would hold up when nanotubes were assembled into a macroscopic system. Then Jianping Lu, a physicist at the University of North Carolina at Chapel Hill, calculated that electrons could travel down a wire of perfectly aligned, overlapping carbon nanotubes with almost no loss of energy.

Smalley’s group has already produced 100-meter-long fibers consisting of well-aligned nanotubes. But the fibers are mixtures of 150 different types of nanotubes, which limits their conductivity. The best wire would consist of just one kind of nanotube—ideally the so-called 5,5-armchair nanotube, named for the arrangement of its carbon atoms. Existing production techniques generate multiple types of nanotubes, indiscriminately. But Smalley believes that adding tiny bits of a single carbon nanotube at the beginning of the process could catalyze the production of huge numbers of identical nanotubes—in essence, “cloning” the original tube.

Silicon Photonics

OPTOELECTRONICS Making the material of computer chips emit light could speed data flow. By Neil Savage



This silicon chip emits laser light.

COURTESY OF YUHUANG WANG/RICE UNIVERSITY (WIRES) COURTESY OF INTEL (SILICON)

The Internet lives on beams of light. One hair-thin glass fiber can carry as much data as thousands of copper wires. But inside your computer, copper still rules. The advantages of light haven’t translated from long-distance connections on the Internet to the short jump between computer chips, in part because the lasers used in optical communications are made from exotic semiconductors incompatible with the standard processes for making silicon computer chips. As computers get faster and faster, they’re nearing the physical limit of copper’s ability to carry more information, and they’ll need something like the fiber-optic network in order to keep improving at the rate we’ve come to expect.

Getting silicon to emit light could be the solution. A light signal’s frequency is much higher than an electrical signal’s, so it can carry thousands of times as much information. Light also overcomes another problem with electrical signals; as transistors get closer together, the electrical signals passing through them start to interfere with each other, like radio stations broadcasting at the same frequency. But turning silicon into a light emitter has proved an extraordinarily difficult challenge. The problem is rooted in an energy-level mismatch between silicon’s electrons and its positively charged “holes” (electron vacancies in its crystal structure): when an electron meets a hole, it’s more likely to release its excess energy as vibration than as light.

But last fall, a team at the University of California, Los Angeles, became the first to make a laser out of silicon. In February, Intel scientists upped the ante, reporting a silicon laser that put out a continuous instead of a pulsed beam, a necessity for data communications. “Once you identify the right piece of physics, everything falls into place,” says UCLA electrical-engineering professor Bahram Jalali, who made the first silicon laser.

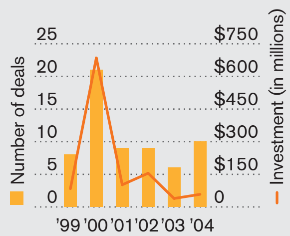
The right piece of physics is the Raman effect. Some photons of light that pass through a material pick up energy from the natural vibration of its atoms and change to another frequency. Jalali fires light from a nonsilicon laser into silicon. Because of the Raman effect, the photons emerge as a laser beam at a different frequency. This Raman laser is “a fundamental scientific break-

through," says Mario Paniccia, director of Intel's Photonics Technology Lab, which is working to create the devices needed for optical communications in silicon. In addition to building a laser, he and his colleagues created a silicon modulator, which allows them to encode data onto a light beam by making it stronger or weaker. Paniccia's group is working to more than double the speed at which it can modulate a beam. A multibillion-dollar infrastructure is already in place for making silicon chips, so Intel believes silicon lasers will be a cost-effective way to raise the computing speed limit.

Photonics-based interconnects between chips should start to appear in about five years, researchers say. The ultimate goal is to enable light-wave communication between components on the same chip, which is several years further out. Philippe Fauchet, professor of optics at the University of Rochester, believes on-chip optical communications will require a silicon laser powered by electricity, which would be cheaper and less complicated than one that depends on an external laser. If such a laser can be built, it will mean that everything from supercomputers on opposite sides of the globe down to the tiniest transistors can talk to each other at the speed of light.

Venture Investment in Photonics Companies

Funding of photonics startups peaked with the bubble in 2000.



SOURCE: PRICEWATERHOUSE COOPERS/THOMSON VENTURE ECONOMICS/NATIONAL VENTURE CAPITAL ASSOCIATION

Metabolomics

MEDICINE A new diagnostic tool could mean spotting diseases earlier and more easily. By Corie Lok

In their quest to develop more-accurate medical diagnostic tests, researchers are turning to a new field called metabolomics–the analysis of the thousands of small molecules such as sugars and fats that are the products of metabolism. If metabolomic information can be translated into diagnostic tests, it could provide earlier, faster, and more accurate diagnoses for many diseases.

Doctors have been measuring a few metabolites for decades to tell what's wrong with patients; glucose for diabetes is a familiar example. Metabolomics researchers, however, sort through hundreds of molecules to tease out a dozen or so that can serve as the signature of a particular disease. "We're hoping that many diseases will have metabolic fingerprints that we can measure," says Maren Laughlin, codirector of a new National Institutes of Health (NIH) metabolomics initiative. Initially, metabolic researchers are hunting for the signatures of conditions such as autism and Huntington's disease.

Metabolomics is, in some ways, a natural offshoot of recent advances in genomics and proteomics, which have allowed researchers to begin to identify many of the genes and proteins involved in diseases. Now researchers are realizing that they need to study metabolites in the same systematic fashion to get a complete picture of the body's processes. And new software and increasingly powerful computers are helping them do it.

Magnetic-Resonance Force Microscopy

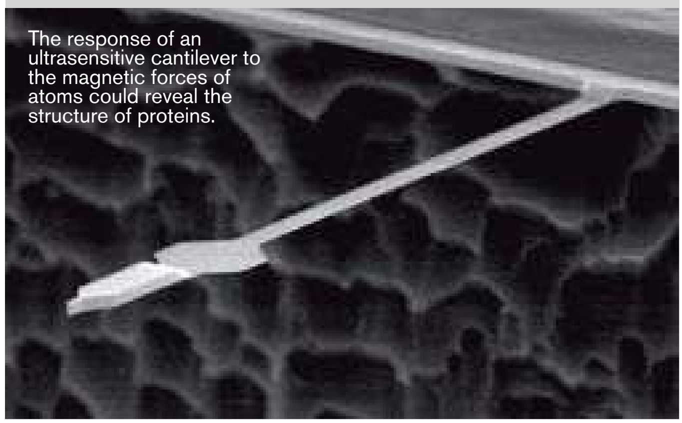
IMAGING The promise is a 3-D view of the molecular world. By David Rotman

In nanotechnology and molecular biology, researchers are often severely limited by the inability to observe atoms and molecules in three dimensions. Proteins, for instance, fold into complex patterns that are largely invisible to the biologists trying to work out their functions of the biomolecules.

So researchers are working to develop a tool that could provide a 3-D view of the nanoworld. The technology—called magnetic-resonance force microscopy (MRFM)—is a hybrid of magnetic-resonance imaging (MRI) and atomic force microscopy (AFM), which is widely used in nanotech. Physicists at the IBM Almaden Research Center in San Jose, CA, led by Daniel Rugar, recently used MRFM to detect the faint magnetic signal—the "spin"—of a single electron. While that accomplishment is still far from the goal of a 3-D snapshot of an atom or molecule, it is a critical step in proving that MRFM could perform atomic-scale imaging. MRFM works by dangling a tiny magnetic tip from the end of an ultrasensitive cantilever that bends in response to even an exceedingly small force. Under just the right conditions, the magnetic force between the tip and an electron changes the vibrations of the cantilever in a measurable way. Scanning a molecule in a 3-D raster pattern could, in theory, generate an image.

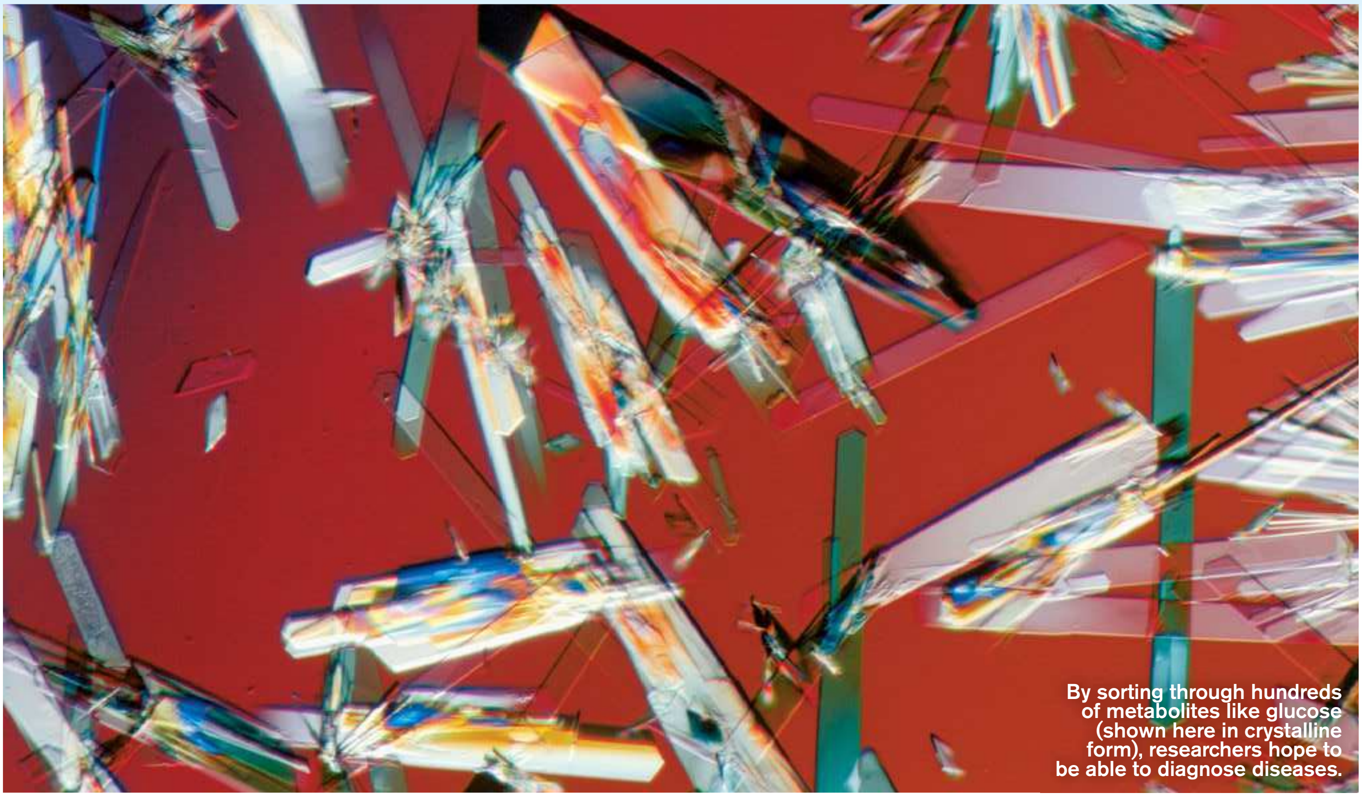
By helping pharmaceutical researchers more directly work out the structures of proteins, MRFM could provide invaluable clues toward the development of safer and more effective drugs. The standard technique for determining the complex three-dimensional structure of proteins involves crystallizing them and then analyzing the diffraction pattern of x-rays that bounce off atoms in the crystal. But not all proteins crystallize, and puzzling out x-ray diffraction patterns is painstaking and tricky.

Researchers at IBM developed the scanning tunneling microscope, which provides images of atoms, and coinvented AFM, which has become a standard tool for atomic-scale manipulation, making possible much of nanotechnology. Whether MRFM will have the same impact is uncertain. But IBM's experimental result is an encouraging signal for those desperate for a clearer, fuller view of the atomic and molecular world.



The response of an ultrasensitive cantilever to the magnetic forces of atoms could reveal the structure of proteins.

COURTESY OF IBM

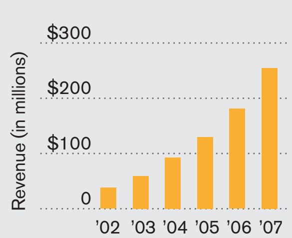


By sorting through hundreds of metabolites like glucose (shown here in crystalline form), researchers hope to be able to diagnose diseases.

METABOLOMICS PHOTOGRAPH BY EYE OF SCIENCE

Metabolomics Market Revenue Forecast

The sale of metabolomic software, analytical hardware, and integrated systems will reach $255 million in 2007.



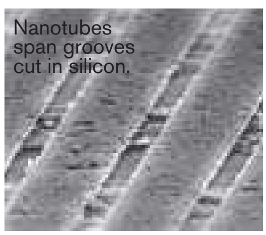
SOURCE: FRONT LINE STRATEGIC CONSULTING

A few small companies aim to have their metabolite-based diagnostic tests on the market within several years. Metabolon of Research Triangle Park, NC, for example, is working with Massachusetts General Hospital to look for metabolic markers for amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, for which there's no definitive blood test. To determine ALS's biochemical profile, the researchers analyzed more than 1,000 molecules in patient blood samples. Using new software to sift through the mountains of data, they found 13 chemicals that showed up consistently at high levels in ALS patients. If larger human trials confirm this 13-chemical profile to be an accurate ALS indicator, it could form the basis of a quick and easy blood test for the deadly disease. Another company, Phenomenome Discoveries of Saskatoon, Saskatchewan, is developing metabolite-based diagnostics for Alzheimer's disease and bipolar disorder.

There are drawbacks to using metabolites as disease markers. Their concentrations tend to fluctuate, since they're heavily influenced by diet; doctors will therefore need to make sure samples are taken from patients under the proper conditions. But that's true of many existing diagnostic tests, says Arthur Castle, the other codirector of the NIH metabolomics initiative. Metabolites may also prove not to be the best markers for every disease; in some cases, analysis of proteins may give a more reliable diagnosis. But metabolomics will give researchers a more comprehensive look at the complex changes under way in hundreds of molecules as a disease begins to develop—which can't help but add to our store of medical knowledge.

Universal Memory

NANOELECTRONICS Nanotubes make possible ultradense data storage. By Gregory T. Huang



Nanotubes span grooves cut in silicon.

COURTESY OF NANTERO

Nantero CEO Greg Schmergel holds a circular wafer of silicon, about the size of a compact disc, sealed in an acrylic container. It's a piece of hardware that stores 10 billion bits of digital information, but what's remarkable about it is the way it does it. Each bit is encoded not by the electric charge on a circuit element, as in conventional electronic memory, nor by the direction of a magnetic field, as in hard drives, but by the physical orientation of nanoscale structures. This technology could eventually allow vastly greater amounts of data to be stored on computers and mobile devices. Experts estimate that within 20 years, you may be able to fit the content of all the DVDs ever made on your laptop computer or store a digital file containing every conversation you have ever had on a handheld device.

Nantero's approach is part of a broader effort to develop "universal memory"—next-generation memory systems that are ultradense and low power and could replace everything from the flash memory in digital cameras to hard drives. Nantero's technology is based on research that the Woburn, MA, company's chief scientist, Thomas Rueckes, did as a graduate student at Harvard University. Rueckes noted that no existing memory technologies seemed likely to prove adequate in the long run. Static and dynamic random-access memory (RAM), used in laptops and PCs, are fast but require too much space and power; flash memory is dense and nonvolatile—it doesn't need power to hold data—but is too slow for computers. "We were thinking of a memory that combines all the advantages," says Rueckes.

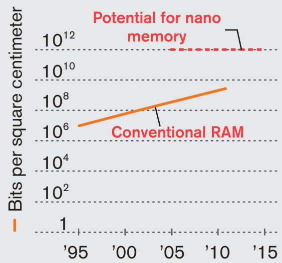
The solution: a memory each of whose cells is made of carbon nanotubes, each less than one-ten-thousandth the width of a human hair and suspended a few nanometers above an electrode. This default position, with no electric current flow between the nanotubes and the electrode, represents a digital *0*. When a small voltage is applied to the cell, the nanotubes sag in the middle, touch the electrode, and complete a circuit—storing a digital *1*. The nanotubes stay where they are even when the voltage is switched off. That could mean instant-on PCs and possibly the end of flash memory; the technology's high storage density would also bring much larger memory capacities to mobile devices. Nantero claims that the ultimate refinement of the technology, where each nanotube encodes one bit, would enable storage of trillions of bits per square centimeter—thousands of times denser than what is possible today. (By comparison, a typical DVD holds less than 50 billion bits total.) The company is not yet close to that limit, however; its prototypes store only about 100 million bits per square centimeter.

Nantero has partnered with chip makers such as Milpitas, CA–based LSI Logic to integrate its nanotube memory with silicon circuitry. The memory sits on top of a layer of conventional transistors that read and write data, and the nanotubes are processed so that they don't contaminate the accessing circuits. By late 2006, Schmergel predicts, Nantero's partners should have produced samples of nanotube memory chips. Early applications may come in laptops and PDAs. Ultimately, however, the goal is to replace all memory and disk storage in all computers.

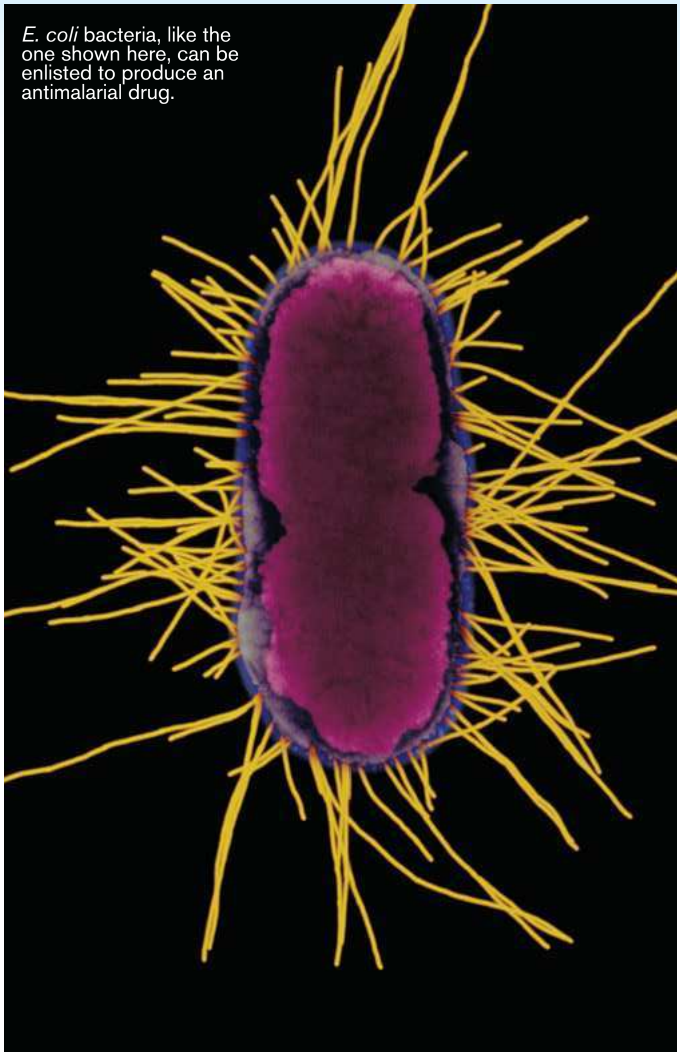
Suspending nanotubes is not the only way to build a universal memory. Other strategies include magnetic random-access memory, which Motorola and IBM and are pursuing, and molecular memory, where Hewlett-Packard is a research leader. But industry experts are watching Nantero's progress with cautious optimism. "They have a very good approach, and it's further along than any other," says Ahmed Busnaina, professor of electrical engineering at Northeastern University and director of the National Science Foundation–funded Center for High-Rate Nanomanufacturing. If successful, this new kind of memory could put a world of data at your fingertips instantly, wherever you go.

Memory Capacity Timeline

The storage capacity of nanomemory has the potential to dwarf that of today's semiconductor RAM technology.



SOURCE: SEMATECH



E. coli bacteria, like the one shown here, can be enlisted to produce an antimalarial drug.

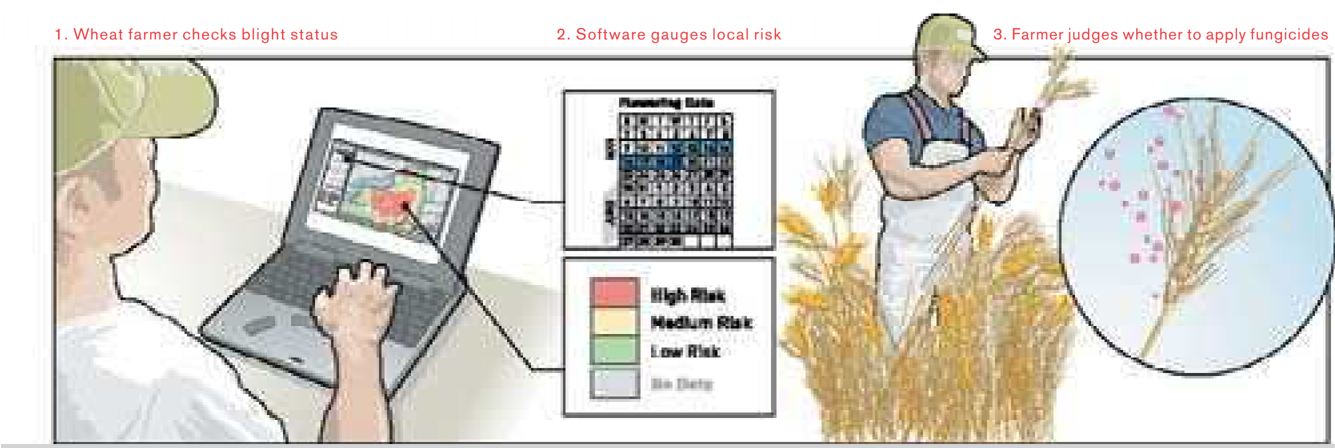
BACTERIAL FACTORIES PHOTOGRAPH BY KWANGSHIN KIM

Bacterial Factories

PHARMACEUTICALS Overhauling a microbe's metabolism could yield a cheap malaria drug.

By Erika Jonietz

In the valleys of central China, a fernlike weed called sweet wormwood grows in fields formerly dedicated to corn. The plant is the only source of artemisinin, a drug that is nearly 100 percent effective against malaria. But even with more farmers planting the crop, demand for artemisinin exceeds supply, driving its cost out of reach for many of the 500 million afflicted with malaria every year. University of California, Berkeley, bioengineer Jay Keasling aims to solve the supply problem—and reduce the cost of treatment to less than 25 cents—by mass-producing the compound in specially engineered bacteria.



ENVIROMATICS ILLUSTRATION BY +ISM

Enviromatics

ENVIRONMENT Computer forecasts enhance farm production and species diversity. By Wade Roush

Environmental scientists think of computers as old friends. They've long used them to crunch the data they collect in the field, whether to map the habitats of endangered species or predict the effects of greenhouse gas emissions on the global climate. But three trends are pushing information technology from the periphery of environmental studies to its very core, according to the proponents of a new field called environmental informatics, or enviromatics.

First, there's a fresh avalanche of raw data about the environment, a product of networked sensors that monitor ecosystems in real time. Second, there's the rise of Internet standards such as the Extensible Markup Language (XML), which can tie together data stored in varying formats in different locations. The third trend—the decreasing cost of computing power—means that researchers can use inexpensive desktop machines to run analyses and simulations that once required supercomputers. Just as the invention of fast gene sequencers a decade ago gave rise to bioinformatics, a new wealth of data about the oceans, the atmosphere, and the land is leading to a wider embrace of sensing, simulation, and mapping tools—and hopefully to more reliable predictions about the future.

Environmental modeling, of course, is nothing new: the ratification of the Kyoto Protocol was spurred in part by global climate models that predict average temperature increases of 1 °C to 6 °C over the next century. But such large-scale, long-range climate models don't help with more immediate and local questions—such as whether the humidity this month in Butler County, PA, means that farmers should apply fungicides early to prevent infections. At Pennsylvania State University's Center for Environmental Informatics, researcher Douglas Miller is pouring data from weather stations throughout the wheat-growing states into a Web-based program that can predict where a devastating wheat fungus infection called fusarium head blight may strike next. Farmers can log into a website, enter their locations and the flowering dates of their crops, and get local maps showing color-coded levels of risk. "We're putting environmental information into people's hands so they can make decisions," says Miller.

Enviromatics is even helping to manage urban growth. In San Diego County, officials compiled a detailed geographical and biological database mapping which vernal pools—basins that fill with rainwater in the winter and spring—harbor the most-endangered strains of species such as the San Diego fairy shrimp and therefore deserve the most protection. Science is rarely the main driver of land management or other decisions affecting the natural environment, but enviromatics may make it harder than ever for politicians to skirt the long-term implications of their decisions.

Keasling's efforts are an example of metabolic engineering, a field in which researchers try to optimize the complex processes whereby a cell produces or breaks down a particular substance. These processes rely on the step-by-step direction of genes; changing even one gene can alter the outcome. Most metabolic engineering has previously focused on modifying a cell's natural processes by inserting, mutating, or deleting a few key genes. According to James Collins, a biological engineer at Boston University, "what Jay is doing is a bit more radical": creating entirely new metabolic pathways by integrating multiple genes from different organisms into a host microbe.

Keasling began his artemisinin project by inserting a set of yeast genes into the common bacterium *E. coli.* These genes induce the bacterium to make the chemical precursor to terpenes—the family of compounds to which artemisinin belongs. Adding in another two genes causes the bacterium to make a specific artemisinin precursor. Introducing a few more genes from sweet wormwood should get the microbe to make artemisinic acid, which is one simple chemical step away from artemisinin. But since *E. coli* don't normally produce these chemicals, each step of the process will have to be carefully contrived and optimized. "There's a lot of engineering still," says Keasling.

A $42.6 million grant from the Bill and Melinda Gates Foundation should help. In December, the foundation awarded the money to Keasling, his Emeryville, CA, startup Amyris Biotechnologies, and San Francisco's Institute for OneWorld Health, a nonprofit that aims to secure U.S. Food and Drug Administration approval for bacteria-derived artemisinin within five years.

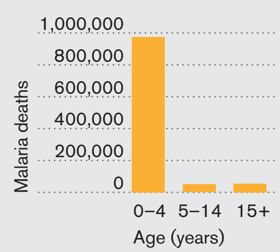
The promise of bacterial factories doesn't end with artemisinin. Amyris Biotechnologies hopes to adapt Keasling's terpene

precursor pathway to make prostratin, a promising anti-HIV compound found in the bark of the mamala tree on Samoa. With different alterations to the pathway, bacteria could make paclitaxel, the breast cancer drug sold under the brand Taxol and now isolated from yew trees.

Ultimately, Keasling believes, new technologies for analyzing and understanding cellular pathways will enable researchers to engineer microbes to produce a huge range of chemicals, from drugs to plastics. And unlike conventional chemical engineering, bacteria do their job cleanly, without requiring or producing environmentally harmful compounds. "We've got all these great tools," Keasling says. "Now we can start to put these to use to solve this one particular problem: how to engineer a cell to do the kinds of chemistries that you want it to do."

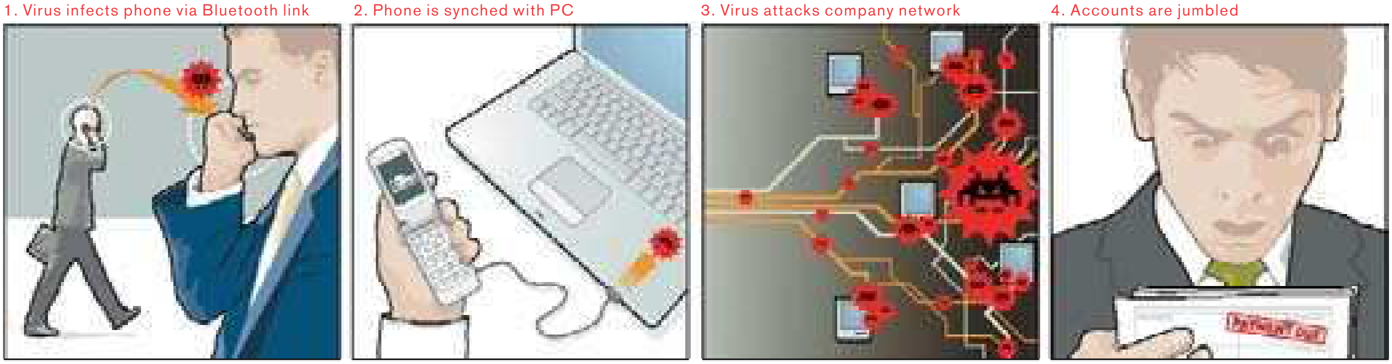
Malaria Impact

The vast majority of malaria victims are children under five who live in Africa.



SOURCE: WORLD HEALTH ORGANIZATION

1. Virus infects phone via Bluetooth link
2. Phone is synched with PC
3. Virus attacks company network
4. Accounts are jumbled



CELL-PHONE VIRUSES ILLUSTRATION BY +ISM

Cell-Phone Viruses

TELECOM Wireless devices catch bad code through the air and then infect supposedly secure computer systems. By Stu Hutson

ValleZ has released a digital epidemic—or maybe he's delivered an early inoculation.

ValleZ is the online handle of a 24-year-old computer programmer from Spain who, last June, wrote the first malicious program targeting cellular phones, the Cabir worm. Now, security experts fear that the rush to integrate cell phones into every aspect of our daily lives might make them the perfect carriers for digital diseases. Bruce Schneier, founder and chief technology officer of Counterpane Internet Security in Mountain View, CA, assesses the threat bluntly: "We're screwed," he says.

Or maybe not. ValleZ is a member of an international cabal of programmers called 29A, which specializes in malicious software, or "malware." These "ethical hobbyists" send their creations to security labs so that experts can research cures. "[Cabir] was a manner of saying that the antiviral people should be watching out for this," says ValleZ, whom *Technology Review* tracked down via e-mail.

ValleZ shared the code for his original, nonmalicious version of the worm with other members of 29A. Shortly after, it was passed to a Brazilian programmer who posted his own variation on his website in December. Now, bad guys everywhere are spinning off new versions that are melded with other malware that locks up phones or autodials obscure numbers. As of March, the Helsinki, Finland–based security company F-Secure reported that 15 variations of Cabir had popped up in 14 countries.

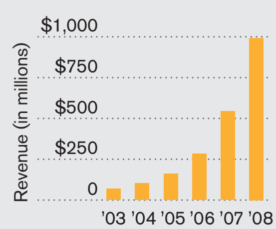
Cabir spreads like an airborne disease through Bluetooth wireless connections, a popular means of transferring data at close proximity between cell phones and everything from other phones to car GPS navigation systems. Even antiviral researchers have found themselves worrying that viruses under examination might spread wirelessly to mobile devices outside their labs' doors. Travis Witteveen, vice president of F-Secure's North American division, says his company now runs its main mobile-security lab out of an old military bomb shelter.

The cell-phone worm's task could be as simple as swiping your address book or spewing out costly and annoying text-message spam. Or it could mount a "denial of service" attack on your wireless-service provider by making your phone rapidly dial many numbers in succession. As people start using their "smart" cell phones to tap into computer networks, the damage caused by malware could grow more severe. If, as promised, cell phones soon begin to serve as payment devices, mobile malware that nabs your identity and taps directly into your credit line could follow. Theoretically, a corporate accountant's phone could pick up a worm and, when synched to a PC, let it loose on the company's network, jumbling accounts.

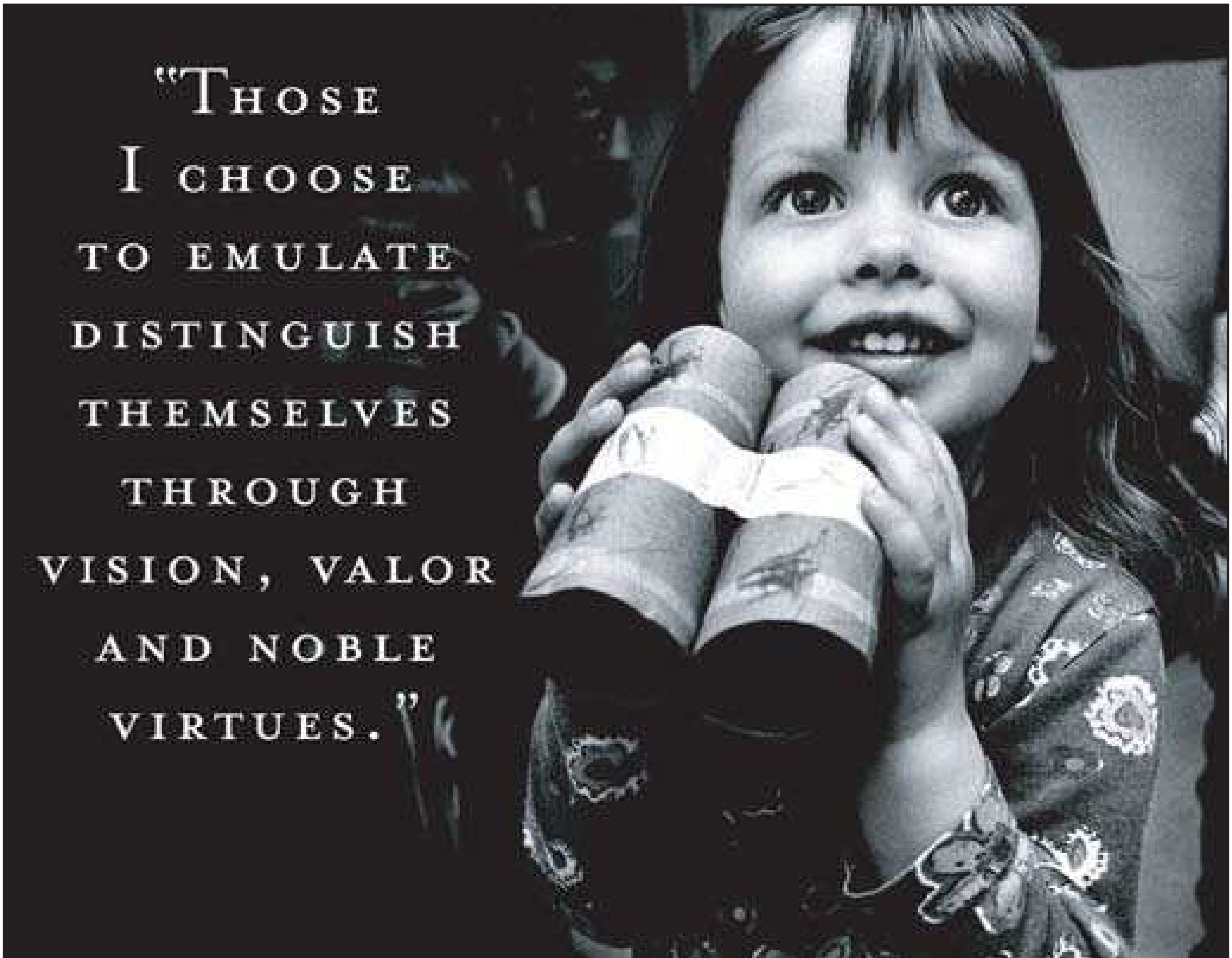
And mobile malware will be able to infect systems not vulnerable to conventional viruses. A car owner could link her Bluetooth-enabled phone to her dashboard computer, so that she can control

Global Market for Mobile-Phone Security Software

The threat of viruses and break-ins could expand the market for mobile security products tenfold between 2004 and 2008.



SOURCE: IDC



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the phone via buttons on his steering wheel. As she drives down the road, her phone might connect to another in a passing car. Suddenly, her navigation system fails. "This type of threat is probably inevitable," says Schneier. In the future, cars will include computer systems that permit remote diagnosis of problems. They should be kept physically separate from hardware that regulates mechanical systems—performing calibrations, for instance—lest a virus cause steering or brake controls to fail.

Protection against this nascent peril is beginning to appear. Symbian, the company whose mobile-device operating system has been targeted by every cell-phone virus so far, has released a version of its software that grants Bluetooth access only to programs tagged with secure digital IDs. Antiviral software is not currently bundled with the software preinstalled on most privately purchased cell phones and so is found almost exclusively in business-issued phones. But companies like McAfee and InnoPath Software are developing easy ways for individual consumers to download antiviral software. According to research firm IDC, spending on mobile security will leap from around $100 million in 2004 to nearly $1 billion by 2008—with a significant portion going toward antiviral protection.

ValleZ says he's done coding mobile malware—for a little while, at least. Of course, that won't stop others from concocting their own electronic pests. Another, completely new and more virulent mobile virus, CommWarrior, was found in late February. It sends out costly multimedia messages but contains so many bugs that it doesn't pose a major threat. The next malicious piece of code, however, may be neither a warning exercise nor a self-defeating pest but a full-bore attack on the wireless world.

Biomechatronics

PROSTHETICS Mating robotics with the nervous system creates a new generation of artificial limbs that work like the real thing. By Corie Lok

Conventional leg prostheses frequently leave their users, especially above-the-knee amputees, stumbling and falling or walking with abnormal gaits. Hugh Herr, a professor at MIT's Media Laboratory, is building more-reliable prostheses that users can control more precisely. Some of the latest prosthetic knees on the market already have microprocessors built into them that can be programmed to help the limbs move more naturally. But Herr has taken this idea one step further. He has developed a knee with built-in sensors that can measure how far the knee is bent, as well as the amount of force the user applies to it while walking. This artificial knee—recently commercialized by the Icelandic company Össur—also contains a computer chip that analyzes the sensor data to create a model of the user's gait, and adapt the movement and resistance of the knee accordingly.

Now Herr is working to distribute those sensors beyond the knee joint, using them to detect not just the mechanical forces of the body but also neural signals from the muscles near the joint. This work is part of an emerging discipline called biomechatronics, in which researchers are building robotic prostheses that can communicate with users' nervous systems. In five to seven years, predicts Herr, spinal-cord injury patients will move their limbs again by controlling robotic exoskeletons strapped onto them (or at least they will in research settings). Biomechatronics is receiving more attention now in part because of the Iraq War, which is sending a high number of U.S. soldiers home with crippling injuries. Herr, who leads the Media Lab's biomechatronics group, is part of a new $7.2 million research project run by the U.S. Department of Veterans Affairs (VA) to develop new technologies for amputees who lost limbs as the result of combat injuries.

* WWW.TECHNOLOGYREVIEW.COM For summaries of the latest developments on the emerging technologies selected in previous years, enter Keyword: TR10.

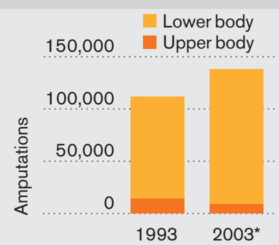
BIOMECHATRONICS ILLUSTRATION BY +ISM

Herr, a double leg amputee, plans on becoming his own first test subject for his latest prosthetic ankle prototype. By early next year, at least three small sensors will be implanted into the muscles of one of his legs below the knee. As Herr flexes his leg muscles in ways that once moved his ankle, these sensors will measure electrical activity in the muscles and transmit that information to a computer chip in the prosthetic ankle, which will translate those impulses into instructions for the ankle's motors. Herr hopes to be able to move the ankle by firing up the residual muscles near the joint and feeling it respond, just as he would with a natural joint. Nor will communication be just one way. Herr should also be able to sense the ankle's position through vibrations emanating from the joint. "We regard this work as extraordinarily promising," says Roy Aaron, a professor of orthopedics at Brown Medical School who is heading up the VA project.

Having lost his lower legs to frostbite while mountain climbing as a teenager, Herr says he's looking forward to trying out the device. "I think it will be quite profound to control my ankles again," he says. Herr's vision for the field is to combine biomechatronics with tissue engineering and create limbs made of both artificial materials and human tissue. Says Herr, "I think, inevitably, we'll end up with hybrid devices." ■

Amputation Trend

According to the U.S. Centers for Disease Control and Prevention, as of 1996, 1.2 million people living in the U.S. had lost limbs. Since then, the diabetes epidemic has driven up the number of amputations.



NUMBER OF U.S. HOSPITAL DISCHARGES INVOLVING AMPUTATIONS. *ESTIMATED. SOURCE: CENTERS FOR DISEASE CONTROL AND PREVENTION

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The Infinite Library

Does Google's plan to digitize millions of print books spell the death of libraries—or their rebirth?

By Wade Roush
Illustration by Bruce McCall

THE BODLEIAN LIBRARY at the University of Oxford in England is the only place you are likely to find an Ethernet port that looks like a book. Built into the ancient bookcases dominating the oldest wing of the 402-year-old library, the brown plastic ports share shelf space with handwritten catalogues of the university's medieval manuscripts and other materials. Some of the volumes are still chained to the shelves, a 17th-century innovation designed to discourage borrowing. But thanks to the Ethernet ports and the university's effort to digitize irreplaceable books like the catalogues—which often contain the only clue to locating an obscure book or manuscript elsewhere in the vast library—users of the Bodleian don't even need to take the books off the shelves. They can simply plug in their laptops, connect to the Internet, and view the pertinent pages online. In fact, anyone with a Web browser can read the catalogues, a privilege once restricted to those fortunate enough to be teaching or studying at Oxford.

The digitization of the world's enormous store of library books—an effort dating to the early 1990s in the United Kingdom, the United States, and elsewhere—has been a slow, expensive, and underfunded process. But last December librarians received a pleasant shock. Search-engine giant Google announced ambitious plans to expand its


PRINTING
FIND
ALL
AUTHORS
BRUCE McCALL

"Google Print" service by converting the full text of millions of library books into searchable Web pages. At the time of the announcement, Google had already signed up five partners, including the libraries at Oxford, Harvard, Stanford, and the University of Michigan, along with the New York Public Library. More are sure to follow.

Most librarians and archivists are ecstatic about the announcement, saying it will likely be remembered as the moment in history when society finally got serious about making knowledge ubiquitous. Brewster Kahle, founder of a nonprofit digital library known as the Internet Archive, calls Google's move "huge....It legitimizes the whole idea of doing large-volume digitization."

But some of the same people, including Kahle, believe Google's efforts and others like it will force libraries and librarians to reëxamine their core principles—including their commitment to spreading knowledge freely. Letting a for-profit organization like Google mediate access to library books, after all, could either open up long-hidden reserves of human wisdom or constitute the first step toward the privatization of the world's literary heritage. "You'd think that if libraries are serious about providing access to high-quality material, the idea of somebody digitizing that stuff very quickly—well, what's not to like?" says Abby Smith, director of programs for the Council on Library and Information Resources, a Washington, DC, nonprofit that helps libraries manage digital transformation. "But some librarians are very concerned about the terms of access and are very concerned that a commercial entity will have control over materials that libraries have collected."

They're also concerned about the book business itself. Publishers and authors count on strict copyright laws to prevent copying and reuse of their intellectual property until after they've recouped their investments. But libraries, which allow many readers to use the same book, have always enjoyed something of an exemption from copyright law. Now the mass digitization of library books threatens to make their content just as portable—or piracy prone, depending on one's point of view—as digital music. And that directly involves libraries in the clash between big media companies and those who would like all information to be free—or at least as cheap as possible.

Whatever happens, transforming millions more books into bits is sure to change the habits of library patrons. What, then, will become of libraries themselves? Once the knowledge now trapped on the printed page moves onto the Web, where people can retrieve it from their homes, offices, and dorm rooms, libraries could turn into lonely caverns inhabited mainly by preservationists. Checking out a library book could become as anachronistic as using a pay phone, visiting a travel agent to book a flight, or sending a handwritten letter by post.

Surprisingly, however, most backers of library digitization expect exactly the opposite effect. They point out that libraries in the United States are gaining users, despite the advent of the Web, and that libraries are being constructed or renovated at an unprecedented rate (architect Rem Koolhaas's Seattle Central Library, for example, is the new jewel of that city's downtown). And they predict that 21st-century citizens will head to their local libraries in even greater numbers, whether to use their free Internet terminals, consult reference specialists, or find physical copies of copyrighted books. (Under the Google model, only snippets from these books will be viewable on the Web, unless their authors and publishers agree otherwise.) And considering that the flood of new digital material will make the job of classifying, cataloguing, and guiding readers to the right texts even more demanding, librarians could become busier than ever.

"I chafe at the presumption that once you digitize, there is nothing left to do," says Donald Waters, a former director of the Digital Library Federation who now oversees the Andrew W. Mellon Foundation's extensive philanthropic investments in projects to enhance scholarly communication. "There is an enormous amount to do, and digitizing is just scratching the surface."

Digitization itself, of course, is no small challenge. Scanning the pages of brittle old books at high speed without damaging them is a problem that's still being addressed, as is the question of how to store and preserve their content once it's in digital form. The Google initiative has also amplified a long-standing debate among librarians, authors, publishers, and technologists over how to guarantee the fullest possible access to digitized books, including those still under copyright (which, in the United States, means everything published after January 1, 1923). The stakes are high, both for Google and for the library community—and the technologies and business agreements being framed now could determine how people use libraries for decades to come.

"Industry has resources to invest that we don't have anymore and never will have," points out Gary Strong, university librarian at the University of California, Los Angeles, which has its own aggressive digitization programs. "And they've come to libraries because we have massive repositories of information. So we're natural partners in this venture, and we all bring different skills to the table. But we're redefining the table itself. Now that we're defining new channels of access, how do we make sure all this information is usable?"

Breaching the Walls

Even for authorized users, access to the Bodleian Library's seven million volumes is anything but instant. If you are an Oxford undergraduate in need of a book, you first send an electronic request to a worker in the library's underground stacks. (Before 2000 or so, you would have handed a written request slip to a librarian, who would have relayed it to the stacks via a 1940s-era network of pneumatic tubes.) The worker locates the book in a warren of movable shelves (a space-saving innovation conceived in 1898 by former British prime minister William Gladstone) and places it in a plastic bin. An ingenious system of conveyor belts and elevators, also built in the 1940s, carries the bin back to any of seven reading rooms, where it is unpacked, and the book is handed over to you.

The process can take anywhere from 30 minutes to several hours. But once you finally have the book, don't even think about taking it back to your dorm room for further study. The Bodleian is a noncirculating legal deposit library, meaning that it is entitled to a free copy of every book published in the United Kingdom and the Republic of Ireland, and it guards those copies jealously. The library takes in tens of thousands of books every year, but the legend is that no book has ever left its walls.

But a *digital* book needn't be loaned out to be shared. And Oxford's various libraries have already created digital images of many of their greatest treasures, from ninth-century illuminated Latin manuscripts to 19th-century children's alphabet books. Most of these images can be examined at high resolution on the Web. The only catch is that scholars have to know what they're looking for in advance, since very few of the digital pages are searchable. Optical character recognition (OCR) technology cannot yet interpret handwritten script, so exposing the content of these books to today's search engines requires typing their texts into separate files linked to the original images. A three-person team at Oxford, in collaboration with librarians at the University of Michigan and 70 other universities, is doing just that for a large collection of early English books, but the entire effort produces searchable text for only 200 books per month. At that rate, making a million books searchable would take more than 400 years.

That's where Google's resources will make a difference. Susan Wojcicki, a product manager at Google's Mountain View, CA, campus and leader of the Google Print project, puts it bluntly: "At Google we're good at doing things at scale."

Google has already copied and indexed some eight billion Web pages, which lends credibility to its claim that it can digitize a big chunk of the 60 million volumes (counting duplicates) held by Harvard, Oxford, Stanford, the University of Michigan, and the New York Public Library in a matter of years. It will be a complex task, but one that is in some ways familiar for the company. "It's not just feeding the books into some kind of digitization machine, but then actually taking the digital files, moving those files around, storing them, compressing them, OCR-ing them, indexing them, and serving them up," points out Wojcicki. "At that point it becomes similar to all of Google's other businesses, where we're managing large amounts of data." But the entire project, Wojcicki admits, hinges on those digitization machines: a fleet of proprietary robotic cameras, still under development, that will turn the digitization of printed books into a true assembly-line process and, in theory, lower the cost to about $10 per book, compared to a minimum of $30 per book today.

Neither Google nor its partner libraries have announced exactly how the process will work. But John Wilkin, associate university librarian at the University of Michigan, says it will go something like this: "We put a whole shelfful of books onto a cart, keeping the order intact. We check them out by waving them under a bar code reader. Overnight, software takes all the bar codes, extracts machine-readable records from the university's electronic catalogue, and sends the records to Google, so they can match them with the books. Then we move the cart into Google's operations room."

This room will contain multiple workstations so that several books can be digitized in parallel. Google is designing the machines to minimize the impact on books, according to Wilkin. "They scan the books in order and return the cart to us," he continues. "We check them back in and mark the records to show they've been scanned. Finally, the digital files are shipped in a raw format to a Google data center and processed to produce something you could use."

The Book Web

Exactly how readers will be able to use the material, however, is still a bit foggy. Google will give each participating library a copy of the books it has digitized while keeping another for itself. Initially, Google will use its copy to augment its existing Google Print program, which mixes relevant snippets from recently published books into the usual results returned by its Web search tool. A user who clicks on a Google Print result is presented with an image of the book page containing his or her keyword, along with links to the sites of retailers selling the print version of the book and keyword-related ads sold to the highest bidders through Google's AdSense program.

"No one thinks the library is disappearing as a physical space. The real question is, what's the 'value proposition' they offer in a digital future?" –Abby Smith

Does it bother librarians that *Moby-Dick* might be served up alongside an ad for the latest Moby CD? "To say we haven't worried about it would be wrong," says Wilkin. "But Google has a 'good citizen' profile. The way they use AdSense doesn't trouble me. And if suddenly access were controlled, and there was a cost to view the materials, we could still offer them for free ourselves, or at least the out-of-copyright materials."

In fact, Google may put the entire texts of these public-domain materials online itself. In the future, Google could even use those materials to create a kind of literary equivalent of the Web, says Wojcicki. "Imagine taking the whole Harvard library and saying, 'Tell me about every book that has this specific person in it.' That in itself would be very powerful for scholars. But then you could start to see linkages between books"—that is, which books cite other books, and in what contexts, in the same way that websites refer to other sites through hyperlinks. "Just imagine the power that that would bring!"

(Wojcicki's example shows how history can, indeed, come full circle. Google founders Larry Page and Sergey Brin devel-

oped BackRub, the predecessor to the Google search engine, while working on an early library digitization project at Stanford that was funded in part by the National Science Foundation's Digital Libraries Initiative. And PageRank, Google's core search algorithm, which orders sites in search results based on the number of other sites that link to them, is simply a computer scientist's version of citation analysis, long used to rate the influence of articles in scholarly print journals.)

The Michigan library, says Wilkin, may do whatever it likes with the digital scans of its own holdings—as long as it doesn't share them with companies that could use them to compete with Google. Such limitations may prove uncomfortable, but most librarians say they can live with them, considering that their holdings wouldn't be digitized at all without Google's help.

Closed Doors?

But others are more cautious about the leap Google's partner libraries are taking. Brewster Kahle, who is often described as an inspiring visionary and sometimes as an impractical idealist, founded the nonprofit Internet Archive in 1996 under the motto "universal access to human knowledge." Since then, the archive has preserved more than a petabyte's worth of Web pages (a petabyte is a million gigabytes), along with 60,000 digital texts, 21,000 live concert recordings, and 24,000 video files, from feature films to news broadcasts. It's all free for the taking at www.archive.org, and as you might guess, Kahle argues that *all* digital library materials should be as freely and openly accessible as physical library materials are now.

That's not such a radical idea; free and open access is exactly what public libraries, as storehouses of printed books and periodicals, have traditionally provided. But the very fact that digital files are so much easier to share than physical books (which scares publishers just as MP3 file sharing scares record companies) could lead to limits on redistribution that prevent libraries from giving patrons as much access to their digital collections as they would like. "Google has brought us to a tipping point that could define how access to the world's literature may proceed," Kahle says.

In Kahle's view, every previous digitization effort has followed one of three paths; with a bit of oratorical flourish, he calls them Door One, Door Two, and Door Three. (Kahle acknowledges up front that his picture is simplified, and that these aren't necessarily the only paths open to libraries today.)

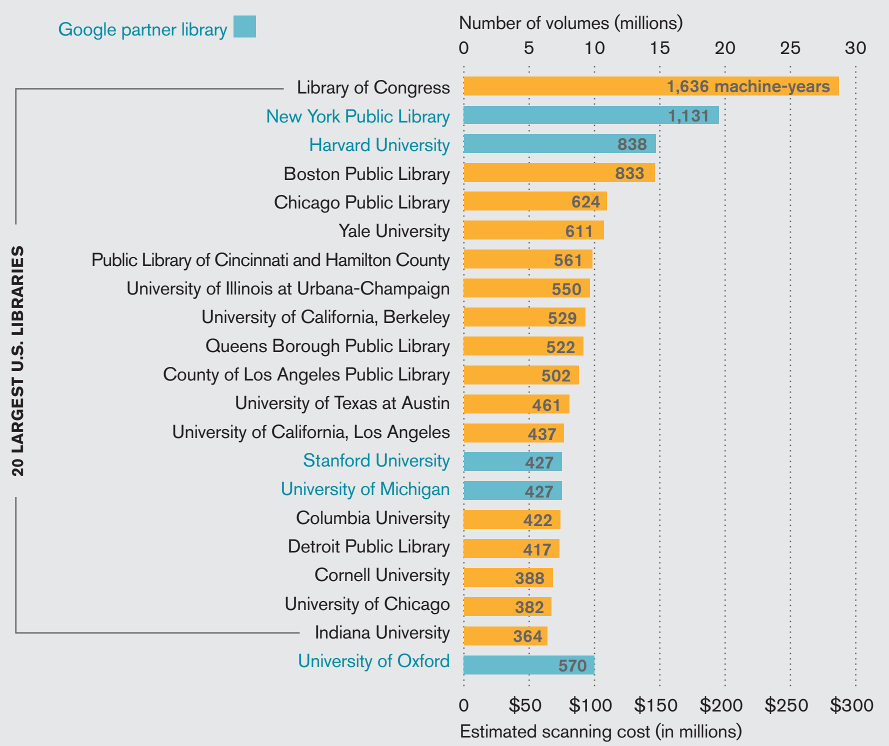
Door One, says Kahle, is epitomized by Corbis, an image-licensing firm owned by Microsoft founder Bill Gates. Since the early 1990s, Corbis has acquired rights to digital reproductions of works from the National Gallery of London, the State Hermitage Museum in St. Petersburg, Russia, the Philadelphia Museum of Art, and more than 15 other museums. In some cases, it's now impossible to use these images without paying Corbis. "This organization got its start by digitizing what was in the public domain and essentially putting it under private control," says Kahle. "The same thing could happen with digital literature. In fact, it's the default case."

Behind Door Two, parallel public and private databases coexist peacefully. Here Kahle cites the Human Genome Project, which culminated in two versions of the DNA sequence of the human genome—a free version produced by government-funded scientists and a private version produced by Rockville, MD–based Celera Genomics and used by pharmaceutical companies to identify new drug candidates. The model has worked well in genomics, and Google seems to be setting out on a similar path, as it keeps one copy of each library's collection for itself and gives away the other. Kahle worries, however, that the restrictions Google imposes on libraries will prevent them from working with other companies or organizations to disseminate digital texts. Libraries might be barred, for example, from contributing material to projects such as the Internet Archive's Bookmobile, a van with satellite Internet access that can download and print any of 20,000 public-domain books.

Door Three, Kahle's favorite, hinges on new partnerships in which private companies offer commercial access to digital

Books to Bits

Google's digitization effort will be expensive and time consuming. The graph below shows how long a single book-scanning machine would take to scan the collections of the largest libraries in the United States, plus the University of Oxford. Of course, the more machines Google uses, the sooner they'll finish.



NOTES: SCANNING MACHINE TIME ASSUMES AN AVERAGE SPEED OF 30 MINUTES PER BOOK. SCANNING COSTS BASED ON AN ESTIMATE OF $10 PER BOOK. SOURCES: AMERICAN LIBRARY ASSOCIATION, LIBRARY OF CONGRESS, NEW YORK PUBLIC LIBRARY

books while public entities, such as libraries, are allowed to provide free access for research and scholarship. Here his main example is the Internet Archive's collaboration with Alexa, a company founded by Kahle himself in 1996 and sold to Amazon in 1999. Alexa ranks websites according to the traffic they attract, and its servers, like Google's, constantly crawl the Internet, making copies of each page they find. But after six months, Alexa donates those copies to the Internet Archive, which preserves them for noncommercial use. "Jeff [Bezos, Amazon's CEO] was okay with the idea that there are some things you can exploit for commercial purposes for a certain amount of time, and then you play the open game," says Kahle. "Libraries and publishing have always existed in the physical world without damaging each other; in fact they support each other. What we would like to see is this tradition not die with this digital transformation."

So which alternative comes closest to Google's plans? Google is no Corbis, says Wojcicki, but is nonetheless limited in what it can share. "Door One was never our intention, nor is it even practical," she says. "And we can't do Door Three, because we're not the rights holders for much of this material. So Door Two is probably where we're headed. We're trying to be as open as possible, but we need to hold to our agreements with different parties."

Precisely to avoid questions about copyright, Oxford librarians have decided that only 19th- and early 20th-century books will be handed over to Google for digitization. "Some of the other libraries, including Harvard, have agreed to have some in-copyright material digitized," says Ronald Milne, acting director of the Bodleian Library. "They are quite brave in taking it on. But we didn't particularly want to go there, because it's such a hassle, and we didn't want to get on the wrong side of the book laws."

At the same time, though, the American Library Association is one of the loudest advocates of proposed legislation to reinforce the "fair use" provisions of federal copyright law, which entitle the public to republish portions of copyrighted works for purposes of commentary or criticism. And two of Google's partner universities—Harvard and Stanford—are also supporters of the Chilling Effects Clearinghouse, a website that monitors allegations of copyright infringement brought against webmasters, bloggers, and other online publishers under the controversial Digital Millennium Copyright Act (DMCA) of 1998. Mass digitization may eventually force a redefinition of fair use, some librarians believe. The more public-domain literature that appears on the Web through Google Print, the greater the likelihood that citizens will demand an equitable but low-cost way to view the much larger mass of copyrighted books. "I think this will be another piece of good pressure, another factor in the whole debate over the DMCA," says Wilkin.

The Mixing Chamber

If you're over 30, today's libraries are probably nothing like the ones you remember from childhood. Enter any major library today and you'll find an armory of computers and a platoon of specialists, from the reference librarians who are expert at accessing online resources, to the acquisitions officers who decide which books, CDs, DVDs, and subscriptions to purchase, to the computer geeks who keep the building's network running.

Digitization and the growing power of the Internet are making all of these people's jobs more complex. Acquisitions experts, for example, can no longer just rely on the traditional quality filter imposed by the publishing industry; they must evaluate a much larger mass of material, from newly digitized print books to the millions of Web pages, blogs, and news sites that are born digital. "On the Internet, publishing is a promiscuous activity," observes Abby Smith of the Council on Library Information and Resources. "Libraries are confused and challenged about how to collect and select from that material."

Then there are the problems of cataloguing and preserving digital holdings. Without the proper "metadata" attached—author, publisher, date, and all the other information that once appeared in libraries' physical card catalogues—a digital book is as good as lost. Yet creating this metadata can be laborious, and no international standard has emerged to govern which kinds of data should be recorded. And considering the limited life span of each new data format or electronic storage medium (have you used a floppy disk lately?), keeping digital materials alive for future generations will, ironically, be much more costly and complicated than simply leaving a paper book on a library shelf.

But even if every book is reduced to a few megabytes of *1*s and *0*s residing on some placeless Web server, libraries themselves will probably endure. "There is no one in the field of librarianship who thinks the library is disappearing as a physical space," says Smith. Seattle's exuberant new Central Library, for example, is built around a four-story spiral ramp that enables an unprecedented immediacy of access to its physical book collection. But at the same time, the library provides 400 public-use computers (compared to 75 in the library that previously occupied the site), buildingwide Wi-Fi access, and a high-tech "mixing chamber" where an interdisciplinary reference team uses an array of print and electronic resources to answer patrons' questions. More than 1.5 million people visited the new library in 2004—almost three times the entire population of Seattle.

"The real question for libraries is, what's the 'value proposition' they offer in a digital future?" says Smith. "I think it will be what it has always been: their ability to scan a large universe of knowledge out there, choose a subset of that, and gather it for description and cataloguing so people can find reliable and authentic information easily." The only difference: librarians will have a much bigger universe to navigate.

Stephen Griffin, the former director of the National Science Foundation's Digital Libraries Initiative (a Clinton-era project that funds a variety of university computer-science studies on managing electronic collections), takes a slightly different view. Ask him how he thinks libraries will function in 2020 or 2050—once Google or its successors have finished digitizing the world's printed knowledge—and he answers from the reader's point of view. "The question is, how will people feel when they walk into libraries," he says. "I hope they feel the same—that this is a very welcoming place that is going to help them to find information that they need. As we bring more technology in, the notion of libraries as places for books may change a bit. But I hope people will always find them a comfortable place for thinking." ■

Wade Roush is a senior editor at Technology Review.

Environmental Heresies

The founder of *The Whole Earth Catalog* believes the environmental movement will soon reverse its position on four core issues.

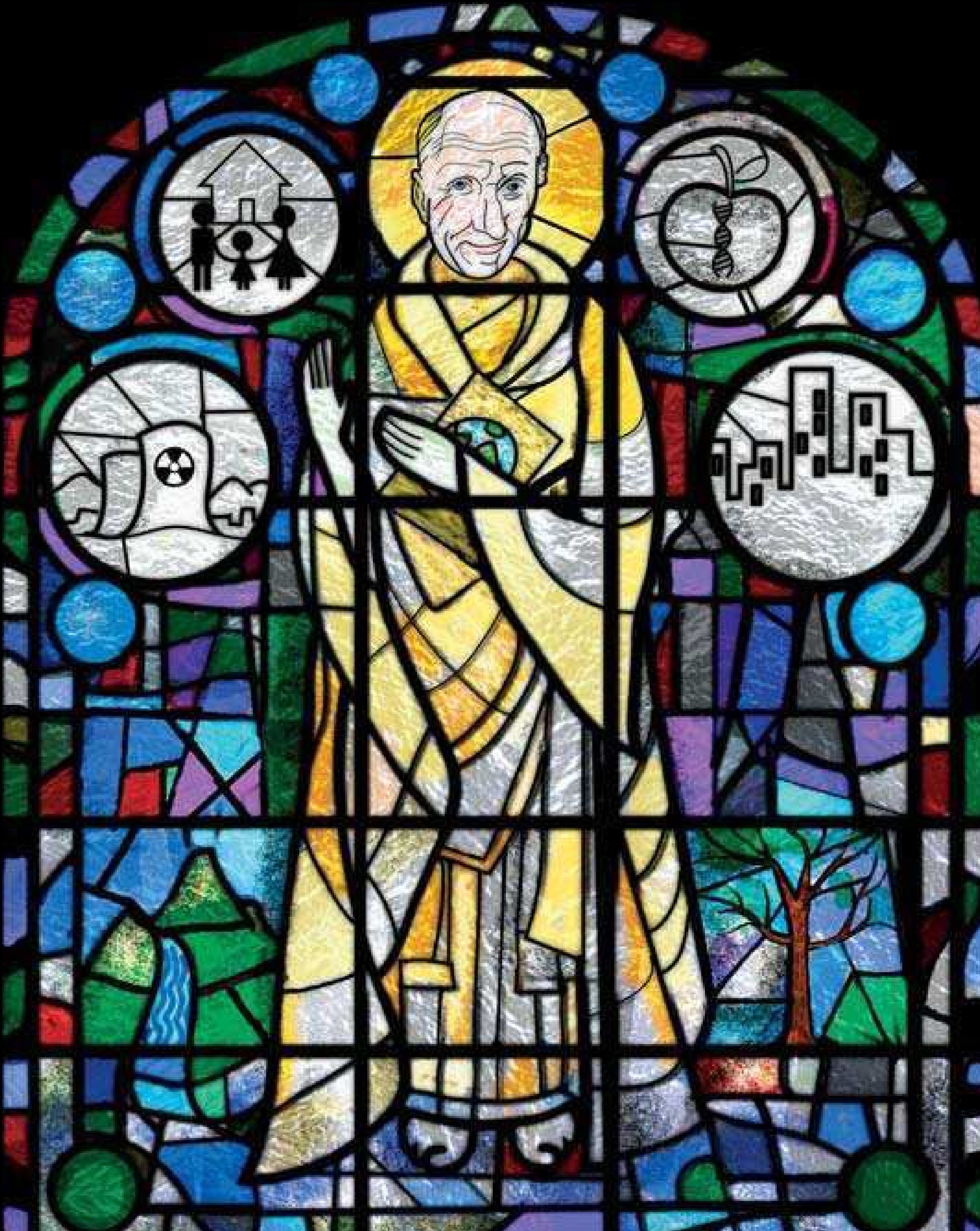
By Stewart Brand
Illustration by Alex Ostroy

OVER THE NEXT TEN YEARS, I predict, the mainstream of the environmental movement will reverse its opinion and activism in four major areas: population growth, urbanization, genetically engineered organisms, and nuclear power.

Reversals of this sort have occurred before. Wildfire went from universal menace in mid-20th century to honored natural force and forestry tool now, from "Only *you* can prevent forest fires!" to let-burn policies and prescribed fires for understory management. The structure of such reversals reveals a hidden strength in the environmental movement and explains why it is likely to keep on growing in influence from decade to decade and perhaps century to century.

The success of the environmental movement is driven by two powerful forces—romanticism and science—that are often in opposition. The romantics identify with natural systems; the scientists study natural systems. The romantics are moralistic, rebellious against the perceived dominant power, and combative against any who appear to stray from the true path. They hate to admit mistakes or change direction. The scientists are ethicalistic, rebellious against any perceived dominant paradigm, and combative against each other. For them, admitting mistakes is what science is.

There are a great many more environmental romantics than there are scientists. That's fortunate, since their inspiration means that most people in developed societies see themselves as environmentalists. But it also means that scientific perceptions are always a minority view, easily ignored, suppressed, or demonized if they don't fit the consensus story line.



Take population growth. For 50 years, the demographers in charge of human population projections for the United Nations released hard numbers that substantiated environmentalists' greatest fears about indefinite exponential population increase. For a while, those projections proved fairly accurate. However, in the 1990s, the U.N. started taking a closer look at fertility patterns, and in 2002, it adopted a new theory that shocked many demographers: human population is leveling off rapidly, even precipitously, in developed countries, with the rest of the world soon to follow. Most environmentalists still haven't got the word. Worldwide, birthrates are in free fall. Around one-third of countries now have birthrates below replacement level (2.1 children per woman) and sinking. Nowhere does the downward trend show signs of leveling off. Nations already in a birth dearth crisis include Japan, Italy, Spain, Germany, and Russia—whose population is now in absolute decline and is expected to be 30 percent lower by 2050. On every part of every continent and in every culture (even Mormon), birthrates are headed down. They reach replacement level and keep on dropping. It turns out that population decrease accelerates downward just as fiercely as population increase accelerated upward, for the same reason. Any variation from the 2.1 rate compounds over time.

That's great news for environmentalists (or it will be when finally noticed), but they need to recognize what caused the turnaround. The world population growth rate actually peaked at 2 percent way back in 1968, the very year my old teacher Paul Ehrlich published *The Population Bomb*. The world's women didn't suddenly have fewer kids because of his book, though. They had fewer kids because they moved to town.

Cities are population sinks. Although more children are an asset in the countryside, they're a liability in the city. A global tipping point in urbanization is what stopped the population explosion. As of this year, 50 percent of the world's population lives in cities, with 61 percent expected by 2030. In 1800 it was 3 percent; in 1900 it was 14 percent.

The environmentalist aesthetic is to love villages and despise cities. My mind got changed on the subject a few years ago. Urbanization is the most massive and sudden shift of humanity in its history. Environmentalists will be rewarded if they welcome it and get out in front of it. In every single region in the world, including the U.S., small towns and rural areas are emptying out. The trees and wildlife are returning. Now is the time to put in place permanent protection for those rural environments. Meanwhile, the global population of illegal urban squatters—which Robert Neuwirth's book *Shadow Cities* already estimates at a billion—is growing fast. Environmentalists could help ensure that the new dominant human habitat is humane and intrudes on less of the surrounding environment.

Along with rethinking cities, environmentalists will need to rethink biotechnology. One area of biotech with huge promise and some drawbacks is genetic engineering, so far violently rejected by the environmental movement. That rejection is, I think, a mistake. Why was water fluoridization rejected by the political right and "frankenfood" by the political left? The answer, I suspect, is that fluoridization came from government and genetically modified (GM) crops from corporations. If the origins had been reversed—as they could have been—the positions would be reversed, too.

The best way for doubters to control a new technology is to embrace it, lest it remain in the hands of enthusiasts.

A Shrug Is as Good as a Wink

Ignore the origin and look at the technology on its own terms. (This will be easier with the emergence of "open source" genetic engineering, which could work around restrictive corporate patents.) What is its *net* effect on the environment? GM crops are more efficient, giving higher yield on less land with less use of pesticides and herbicides. That's why the Amish, the most technology-suspicious group in America (and the best farmers), have enthusiastically adopted GM crops.

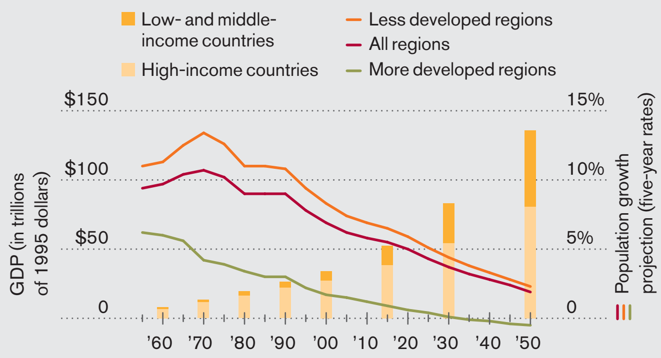
There has yet to be a public debate among environmentalists about genetic engineering. Most of the scare stories that go around (Monarch caterpillars harmed by GM pollen!) have as much substance as urban legends about toxic rat urine on Coke can lids. Solid research is seldom reported widely, partly because no news is not news. A number of leading biologists in the U.S. are also leading environmentalists. I've asked them how worried they are about genetically engineered organisms. Their answer is "Not much," because they know from their own work how robust wild ecologies are in defending against new genes, no matter how exotic. They don't say so in public because they feel that entering the GM debate would strain relations with allies and would distract from their main focus, which is to research and defend biodiversity.

The best way for doubters to control a questionable new technology is to embrace it, lest it remain wholly in the hands of enthusiasts who don't see what's questionable about it. I would love to see what a cadre of ardent environmental scientists could do with genetic engineering. Besides assuring the kind of transparency needed for intelligent regulation, they could direct a powerful new tool at some of the most vexed problems in their field.

For instance, invasive species. About 80 percent of the current mass extinctions of native species are caused by habitat loss, a problem whose cure is well known: identify the crucial habitats and preserve, protect, and restore them. The remaining 20 percent of extinctions are coming from invasive species, with no solution in sight. Kudzu takes over the American South, brown tree snakes take over Guam (up to 5,000 a square kilometer), zebra mussels and mitten crabs take over the U.S. waterways, fire ants

Malthus Was Wrong

As wealth grows and is increasingly distributed toward low-income countries, population growth rates are expected to continue to fall, approaching replacement rates by 2050.



SOURCES: UNITED NATIONS, WORLD BANK

and fiendishly collaborative Argentine ants take over the ground, and not a thing can be done. Volunteers like me get off on yanking up invasive French broom and Cape ivy, but it's just sand castles against a rising tide. I can't wait for some engineered organism, probably microbial, that will target bad actors like zebra mussels and eat them, or interrupt their reproductive pathway, and then die out.

Now we come to the most profound environmental problem of all, the one that trumps everything: global climate change. Its effect on natural systems and on civilization will be a universal permanent disaster. It may be slow and relentless—higher temperature, rising oceans, more extreme weather getting progressively worse over a century. Or it may be "abrupt climate change": an increase of fresh water in the north Atlantic shuts down the Gulf Stream within a decade, and Europe freezes while the rest of the world gets drier and windier. (I was involved in the 2003 Pentagon study on this matter, which spelled out how a climate change like the one 8,200 years ago could occur suddenly.)

Let's Go Nuclear

Can climate change be slowed and catastrophe avoided? They can to the degree that humanity influences climate dynamics. The primary cause of global climate change is our burning of fossil fuels for energy.

So *everything* must be done to increase energy efficiency and decarbonize energy production. Kyoto accords, radical conservation in energy transmission and use, wind energy, solar energy, passive solar, hydroelectric energy, biomass, the whole gamut. But add them all up and it's still only a fraction of enough. Massive carbon "sequestration" (extraction) from the atmosphere, perhaps via biotech, is a widely held hope, but it's just a hope. The only technology ready to fill the gap and stop the carbon dioxide loading of the atmosphere is nuclear power.

Nuclear certainly has problems—accidents, waste storage, high construction costs, and the possible use of its fuel in weapons. It also has advantages besides the overwhelming one of being atmospherically clean. The industry is mature, with a half-century of experience and ever improved engineering behind it. Problematic early reactors like the ones at Three Mile Island and Chernobyl can be supplanted by new, smaller-scale, meltdown-proof reactors like the ones that use the pebble-bed design. Nuclear power plants are very high yield, with low-cost fuel. Finally, they offer the best avenue to a "hydrogen economy," combining high energy and high heat in one place for optimal hydrogen generation.

The storage of radioactive waste is a surmountable problem *(see "A New Vision for Nuclear Waste," December 2004)*. Many reactors now have fields of dry-storage casks nearby. Those casks are transportable. It would be prudent to move them into well-guarded centralized locations. Many nations address the waste storage problem by reprocessing their spent fuel, but that has the side effect of producing material that can be used in weapons. One solution would be a global supplier of reactor fuel, which takes back spent fuel from customers around the world for reprocessing. That's the kind of idea that can go from "Impractical!" to "Necessary!" in a season, depending on world events.

The environmental movement has a quasi-religious aversion to nuclear energy. The few prominent environmentalists who have spoken out in its favor—Gaia theorist James Lovelock, Greenpeace cofounder Patrick Moore, Friend of the Earth Hugh Montefiore—have been privately anathematized by other environmentalists. Public excoriation, however, would invite public debate, which so far has not been welcome.

Nuclear could go either way. It would take only one more Chernobyl-type event in Russia's older reactors (all too possible, given the poor state of oversight there) to make the nuclear taboo permanent, to the great detriment of the world's atmospheric health. Everything depends on getting new and better nuclear technology designed and built.

Years ago, environmentalists hated cars and wanted to ban them. Then physicist Amory Lovins came along, saw that the automobile was the perfect leverage point for large-scale energy conservation, and set about designing and promoting drastically more efficient cars. Gas-electric hybrid vehicles are now on the road, performing public good. The United States, Lovins says, can be the Saudi Arabia of nega-watts: Americans are so wasteful of energy that their conservation efforts can have an enormous effect. Single-handedly, Lovins converted the environmental movement from loathing of the auto industry to fruitful engagement with it.

Someone could do the same with nuclear power plants. Lovins refuses to. The field is open, and the need is great.

Within the environmental movement, scientists are the radical minority leading the way. They are already transforming the perspective on urbanization and population growth. But their radicalism and leadership will have to increase if humanity is to harness green biotech and step up to its responsibilities for the global climate. The romantics are right, after all: we are indivisible from the earth's natural systems. ■

Stewart Brand founded The Whole Earth Catalog *and cofounded the Well, the first electronic community. His books include* The Media Lab, How Buildings Learn, *and* The Clock of the Long Now. *Today, he works with the Global Business Network and the Long Now Foundation.*

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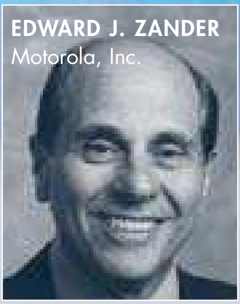

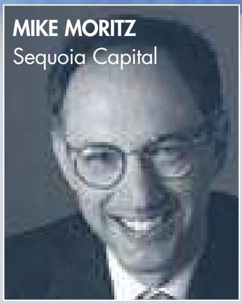

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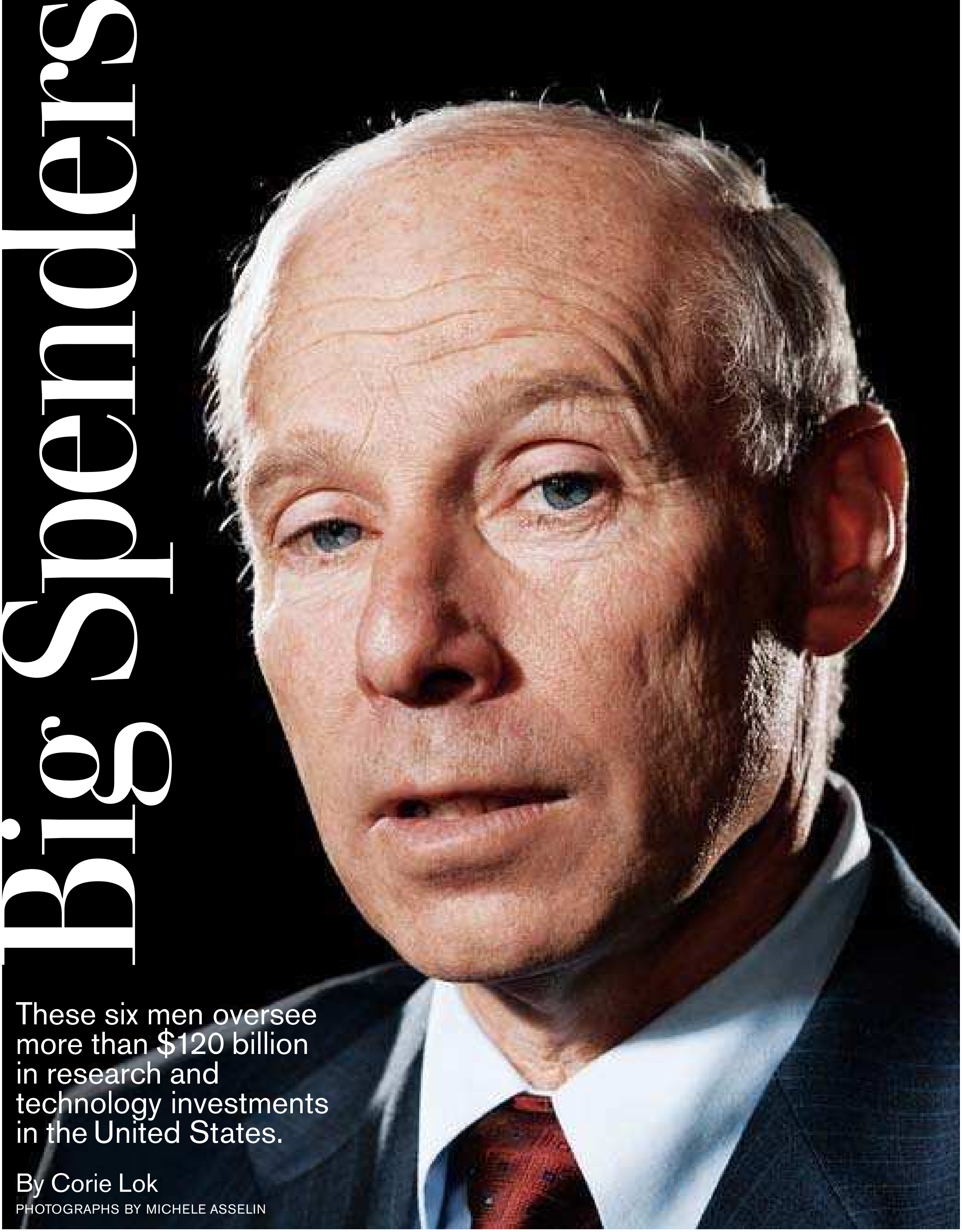


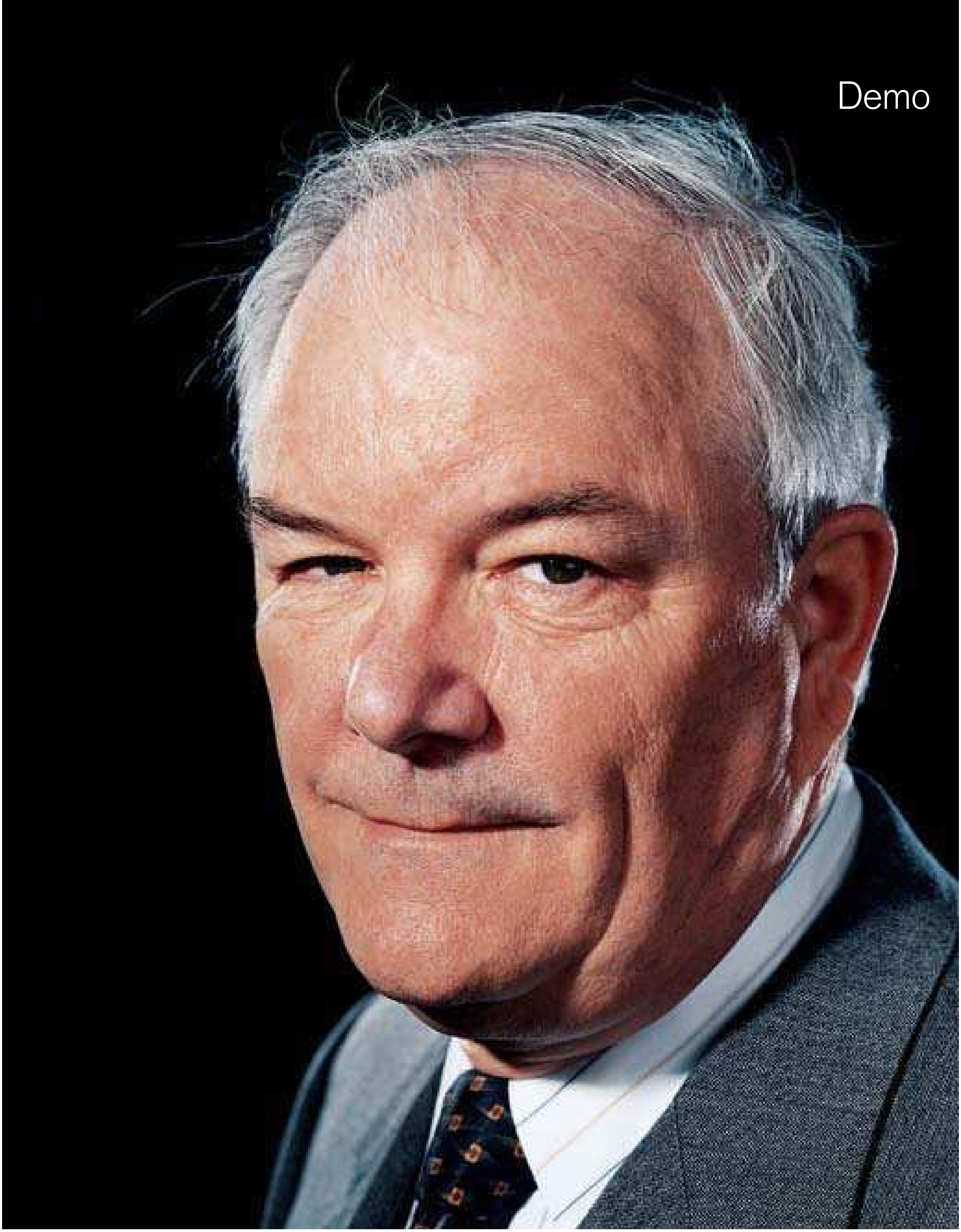
Big Spenders

These six men oversee more than $120 billion in research and technology investments in the United States.

By Corie Lok

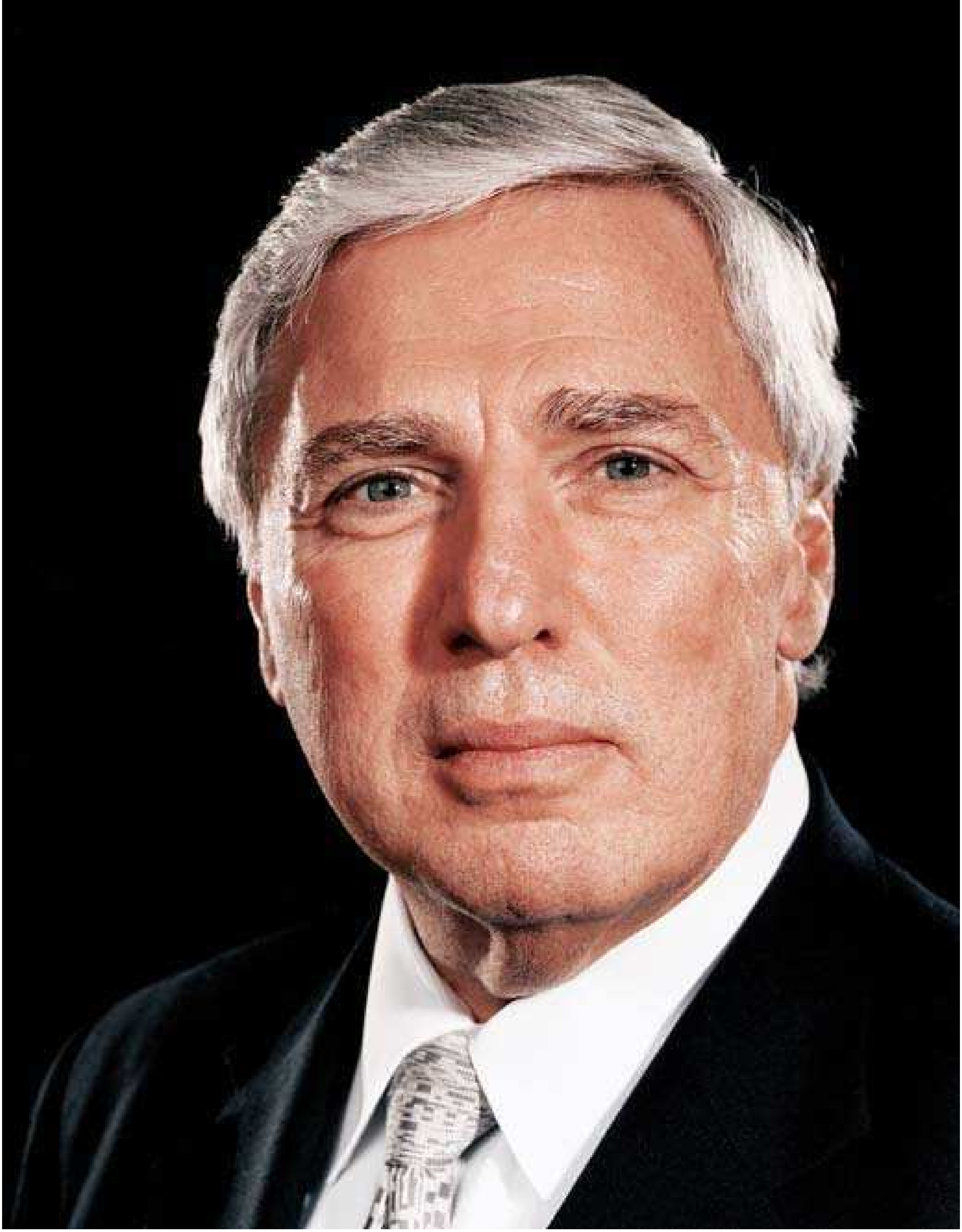
PHOTOGRAPHS BY MICHELE ASSELIN

JOHN LAMATTINA is the president of Pfizer Global Research and Development. Pfizer, headquartered in New York, NY, has the pharmaceutical industry's largest R&D budget—$7.7 billion last year—and one of the largest among all corporations. Trained as a chemist, LaMattina now oversees more than 12,500 scientists at eight major research campuses and other smaller facilities in five countries.

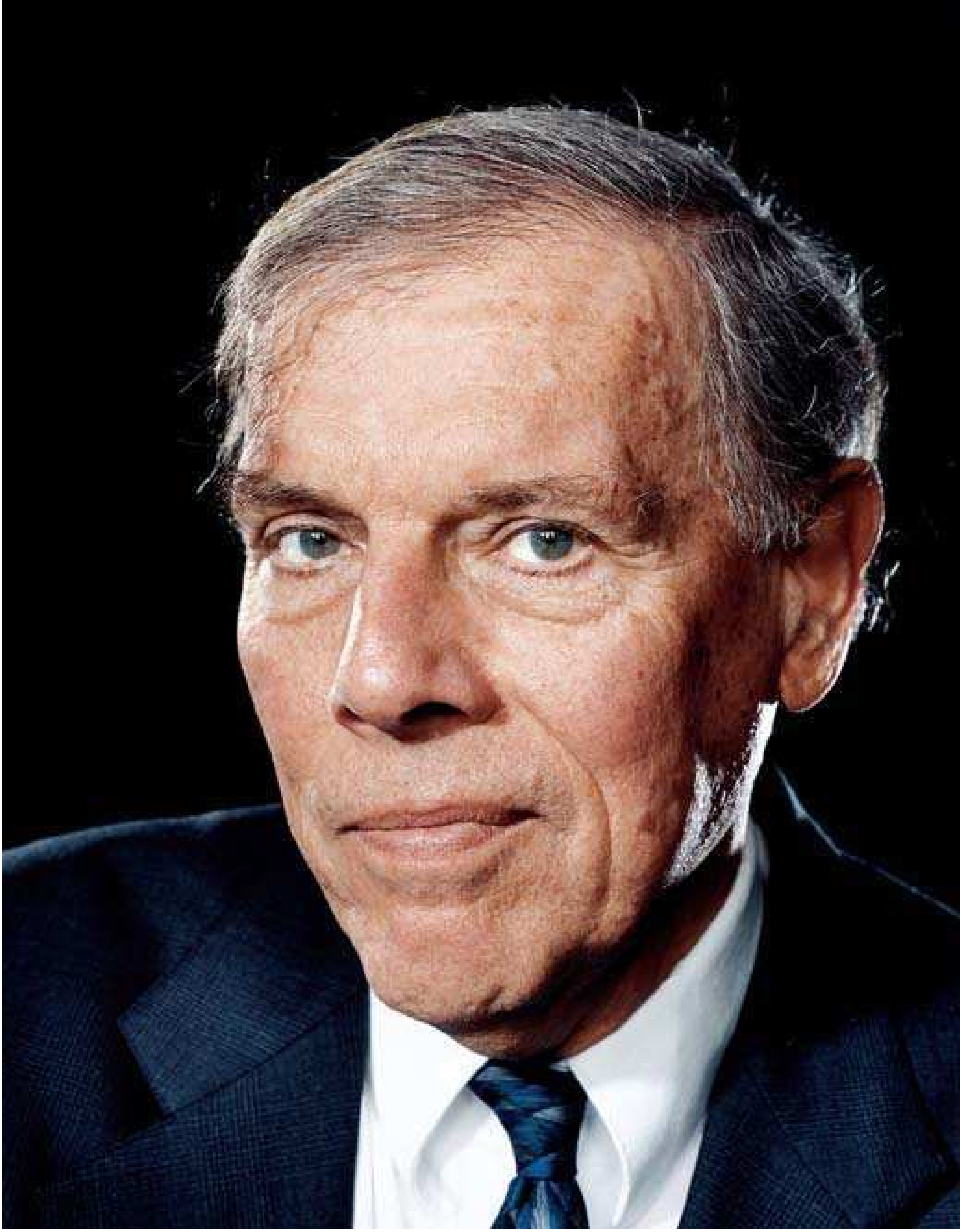


MICHAEL WYNNE is the acting undersecretary of defense for acquisition, technology, and logistics at the U.S. Department of Defense. He advises the secretary and deputy secretary of defense on acquisition, R&D, and advanced-technology matters. The military's budget for R&D and advanced-technology testing and evaluation for fiscal year 2005 is $69 billion.

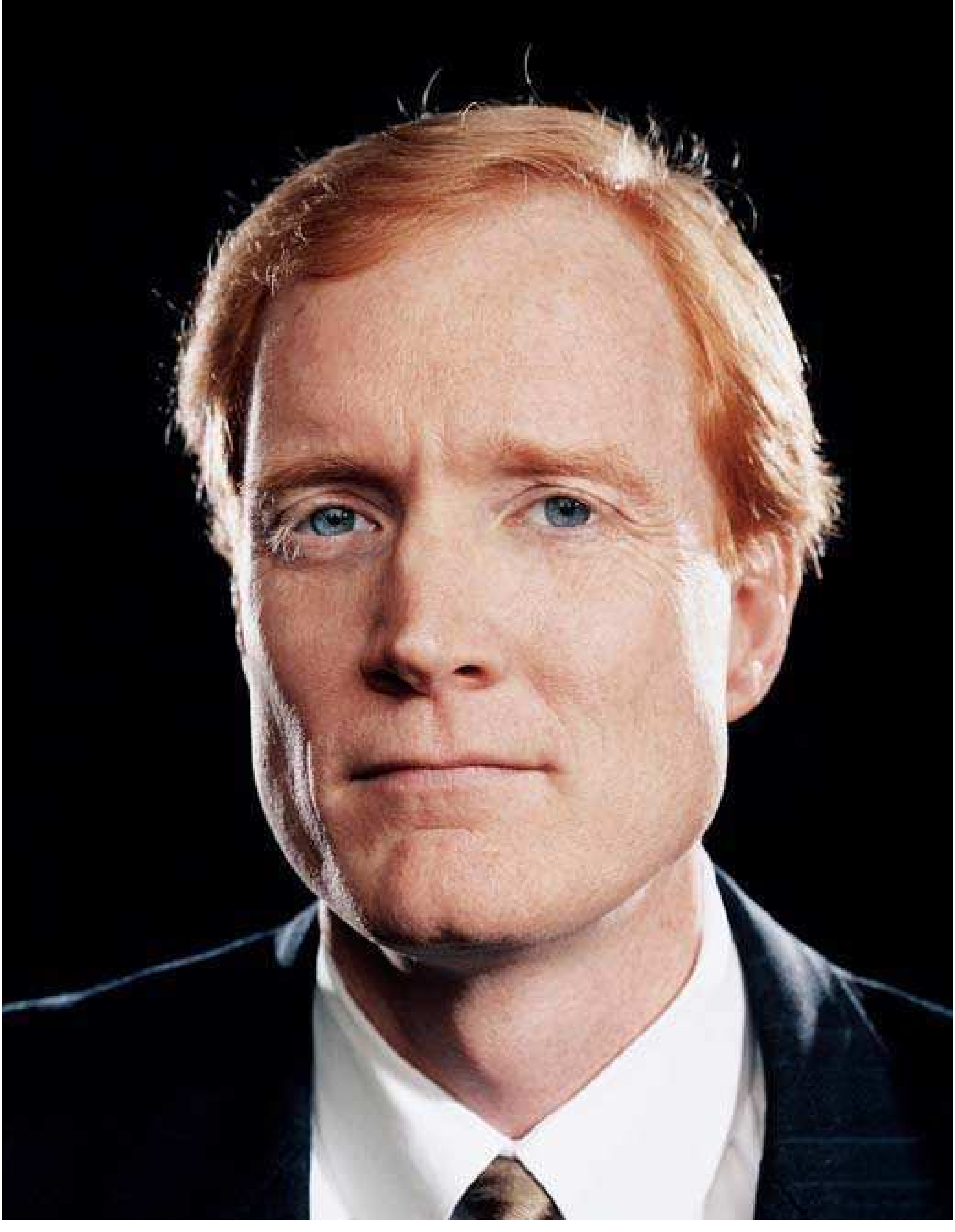
DON VALENTINE is a partner and the founder of Sequoia Capital, a leading technology venture capital firm in Menlo Park, CA. Sequoia completed 30 investment deals last year, making it one of the most active technology venture capital firms. Valentine founded the firm in 1972 and was an original investor in Apple Computer, Atari, and Oracle.



ANDREW VON ESCHENBACH is the director of the National Cancer Institute, the largest institute within the National Institutes of Health, with a 2005 budget of $4.8 billion. He is a urologic surgeon and a cancer survivor. He has made it a goal of his organization to eliminate suffering and death due to cancer by 2015.



THEODORE POEHLER is the vice provost for research at Johns Hopkins University, whose total research budget this year is about $1.2 billion, the largest among U.S. universities. Trained as an electrical engineer, Poehler has a bachelor's and a master's degree and a PhD, all from Johns Hopkins, and has spent almost his entire professional career with the university.



STEVE MCGAW was Cingular Wireless's head of corporate development and the chief negotiator behind its acquisition of AT&T Wireless last year, in a deal worth $41 billion. This was the largest technology acquisition in the United States last year, and it made Cingular the number one U.S. wireless provider. McGaw is now senior vice president, supply chain, at Cingular.

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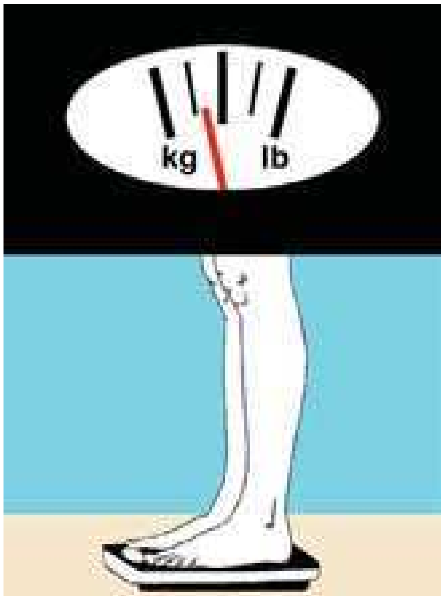
The Trouble with the Meter

Why the metric system may never completely rule

Amid the ideological and religious upheavals of the last 200 years, the metric system has spread around the world as an exemplar of science and rationality. But in both its champions and detractors, it has evoked as much passion as reason.



MARK DANIELSON

Created beginning in 1790 by the French Academy of Sciences at the behest of the revolutionary National Assembly, the metric system reflected a century of measurement reform proposals. The meter was defined by a law of the National Convention in 1793 as one ten-millionth of a quarter-meridian, the distance from the earth's equator to one of its poles. Ken Alder of Northwestern University, studying records in Paris, found that the attempt to measure the meridian mixed painstaking detail with high adventure. It took two French astronomers seven years to measure the distance between Dunkirk, France, and Barcelona, Spain, and Alder's memorable account, *The Measure of All Things*, reveals that one of the men covered up for the other's fudged work. The astronomers knew the earth was slightly flat at the poles–Pierre-Louis Moreau de Maupertuis had proved Newton's prediction in 1736–but thought it otherwise uniform. Survey one meridian, they thought, and you've surveyed them all. They soon learned the lumpiness of reality.

Not only was the earth-based metric system difficult to devise, and flawed: it was also unnecessary. Two Italian scientists, Paolo Agnoli and Giulio D'Agostini, recently noted in a paper that well before the French Revolution, scientists proposed a new unit that was less than a half-centimeter shorter than the current meter. They defined it not by measuring the earth, but by timing a pendulum. The Italian polymath Tito Livio Burattini proposed such a "catholic [i.e., universal] meter" as early as 1675. Burattini noted that a weight swinging on a string the length of his proposed meter returned to its original position in two seconds. The amount of time the weight took to travel from one maximum elevation to the other was one second: a unit that corresponded with the approximate duration of a human heartbeat. Timing a pendulum, even in a vacuum at a controlled temperature, was easier than surveying a meridian, and its deeply human rhythm was satisfying.

Why did the Academy of Sciences take the more difficult course? Because time itself was in play. The Academy was considering the establishment of a decimal-based ten-hour day, with 100 seconds to a minute and 100 minutes to an hour. Besides, France's scientists believed the project would unite humanity in the thrill of common proprietorship of the newly measured globe. After the shortcomings of the meridian-based meter became apparent, a platinum meter bar was presented to the French legislature in June 1799 as an arbitrary basis for the new measurement.

Since 1983, to establish greater precision than any material object allows even in controlled conditions, the 51-nation General Conference on Weights and Measures has defined the meter as the distance traveled by light in a vacuum during a time interval of 1/299,792,458 of a second. The Système International d'Unités (SI) starts with seven basic units–the meter, kilogram, second, ampere, kelvin, mole, and candela–and defines 22 others that include every unit science, technology, and commerce need but money (and even that is now universally decimal).

Elegant as it is, the metric system has provoked spirited resistance. Some countries, including France in the 19th century and the U.K. today, have imposed draconic penalties on recalcitrant vendors; a northeast English grocer was sentenced to probation in 2001 for selling bananas by the pound rather than the kilogram. In the U.S., the government has yielded to opposition even to dual systems of measurement. In 1978, the Federal Highway Administration's policy of adding distances in kilometers to highway signs was reversed following protests of antimetric folk who saw the thin edge of a wedge.

The conflicts over metrication tell a messy truth: no single system of measurements is ideal for all uses. Like any object of human design, a measurement system trades one advantage for another. In its avoidance of thirds, for example, the metric system has no colloquial equivalent of the foot. Decimeters are seldom used; the system skips an order of magnitude from the centimeter to the meter. And liters exceed normal individual human thirst.

On the other hand, the millimeter has its own advantages. Around the thickness of two fingernails, it's the smallest unit we find useful for measuring common objects; a dime is 1.35 mm thick. It avoids the contortions of arithmetic involving sixteenths and thirty-seconds of an inch. Only where objects are regularly divided in half, as in carpentry and the building trades, does the inch come into its own. *What* is being measured dictates the appeal of the system used to measure it. The metric system has become the world's lingua franca, but traditional measures, rooted in the body and its crafts, are its tenacious vernacular. ■

Reviews

Our reviews use any artifact—a book, a product, a government report, a movie, a research paper—as the occasion for a contemplative essay on some technological controversy.

The Economics of Brains

A collection of research papers touts the promise of neuroeconomics.

BY GREGORY T. HUANG

Traditional economic theory assumes that human beings behave rationally. That is, that they understand their own preferences, make perfectly consistent choices over time, and try to maximize their own well-being. This peculiar assumption has its roots in dusty essays like "Exposition of a New Theory on the Measurement of Risk" (from 1738) by Daniel Bernoulli and scholarly tomes like *Theory of Games and Economic Behavior* by John von Neumann and Oskar Morgenstern (published in 1944). The idea has some validity: traditional economic theory is good at predicting some market behaviors, such as how the demand for products like gasoline will change after a tax hike. But it's not very good at describing more-complex phenomena like stock-price fluctuations or why people gamble against the odds.

The problem, of course, is that people don't always behave rationally. They make decisions based on fear, greed, and envy. They buy plasma TVs and luxury vehicles they can't afford. They don't save enough for retirement. They indulge in risky behavior such as gambling. Economists understand this as well as anyone, but in order to keep their mathematical models tractable, they make simplifying assumptions. Then they try to adjust their equations by adding terms that account for "irrational" behavior. But if economists could develop models that accounted for the subtleties of the human brain, they might be able to predict complex behaviors more accurately. This, in turn, might have any number of practical applications: investment bankers could hedge against financial euphoria like the Internet boom; advertisers could sell products more winningly.

The idea that understanding the brain can inform economics is controversial but not new; for 20 years, behavioral economists have argued that psychology should have a greater influence on the development of economic models. What is new is the use of technology: economists, like other researchers, now have at their disposal powerful tools for observing the brain at work. The most popular tool, functional magnetic resonance imaging (fMRI), has been around since the late 1980s; but only in the past few years has it been used to study decision-making, which is the crux of economic theory.

The result is the emerging field of "neuroeconomics." A flurry of recent papers in scientific and economic journals—reviewed in the *Journal of Economic Literature* by Caltech economics professor Colin Camerer and colleagues—shows how researchers are using the neural basis of decision-making to develop new economic models. At the January meeting of the American Economic Association, the world's largest economics conference, the neuroeconomics sessions were reportedly standing room only. The hope seems to be that biological research will finally help economists make sense of irrationality.

Take recent brain-imaging experiments by Princeton University psychologist Samuel McClure. In the journal *Science*, McClure and colleagues report that when subjects choose short-term monetary rewards, different regions of the brain are active than when they choose long-term ones. People don't "discount" future rewards according to a simple scheme, as many economists have suggested. It seems the brain actually makes short-term and long-term forecasts in different ways. The challenge for economists lies in translating this sort of scientific insight into, say, predictive models of how people plan purchases or make retirement fund decisions.

This Is Your Brain on Money

"Addiction and Cue-Triggered Decision Processes"
By B. Douglas Bernheim and Antonio Rangel
The American Economic Review, December 2004

"Neuroeconomics: How Neuroscience Can Inform Economics"
By Colin Camerer, George Loewenstein, and Dražen Prelec
Journal of Economic Literature, March 2005

"Neurally Reconstructing Expected Utility"
By Brian Knutson and Richard Peterson
Games and Economic Behavior (in press)

"The Adaptive Markets Hypothesis: Market Efficiency from an Evolutionary Perspective"
By Andrew W. Lo
The Journal of Portfolio Management, 30th Anniversary Issue, 2004

"Separate Neural Systems Value Immediate and Delayed Monetary Rewards"
By Samuel M. McClure, David I. Laibson, George Loewenstein, and Jonathan D. Cohen
Science, October 15, 2004

MICHEAL MCLAUGHLIN

If successful, neuroeconomics could help unify the social sciences and natural sciences—all with great societal impact. "We are at the very beginning of something radically new," says Daniel Kahneman, the Princeton University psychologist who won the 2002 Nobel Prize in economics. "Technologically, we can expect that within the next decade or two there will be huge developments. The network of knowledge about the brain is expanding at a tremendous rate. That will certainly affect marketing and political psychology, and it could create a common database that nobody will want to ignore."

Decisions, Decisions

It's an intriguing idea: to rethink economic theory from the ground up, taking into account the workings of the human brain. For now, though, neuroeconomics is far removed from the day-to-day concerns of most financiers or CEOs.

The first thing to remember is that the field is very, very young. Neurological tools are still relatively crude. Brain-imaging techniques such as fMRI and positron emission tomography (PET) measure changes in blood flow and hence reveal the collective activity of thousands of neurons over a period of seconds. An electroencephalogram (EEG) uses electrodes on the scalp to measure the brain's electrical activity on the millisecond time scale, but its spatial resolution is so poor that its use is limited. What's more, imaging studies point out only correlations between brain activity and behavior. One must be careful in drawing neuroscientific conclusions and making economic predictions.

Because their field is so young, and because they are pursuing different goals, economists and neuroscientists working in neuroeconomics sometimes seem to be talking about different things. For instance, Camerer and his colleagues write that "The foundations of economic theory were constructed assuming that details about the functioning of the brain's black box would not be

known....[But now] the study of the brain and nervous system is beginning to allow direct measurement of thoughts and feelings." Most neuroscientists would disagree with the second point. Direct measurement of how groups of neurons interact and which brain areas are active during which physical and mental tasks, yes. But thoughts and feelings are subjective *(see "The Unobservable Mind," February 2005)* and observable only by interpreting data.

In a similar vein, neuroscientists and psychologists have at times equated economic utility—the subjective value of a good or service—with the notions of reward and pleasure. These ideas may be related, but they are certainly not interchangeable. Nevertheless, early mutual confusion about both fields' technical terms and bodies of knowledge is being resolved. "We are rapidly approaching a common language," says Gregory Berns, a neuroscientist at Emory University.

A more fundamental issue for neuroeconomics is this: should economists care? Perhaps understanding how the brain works is more trouble than it's worth. After all, some recent findings are not at first glance very economically enlightening. Anyone who has regretted an impulse purchase, for instance, would be unsurprised to learn that evaluations of immediate and delayed rewards use different parts of the brain. For now, neuroeconomics is subject to the criticisms that plague psychology: that its experiments show what is already intuitively obvious, and its models are descriptive, not quantitative. But Stanford psychologist Brian Knutson and psychiatrist Richard Peterson are trying to answer that criticism. Their paper in a forthcoming issue of *Games and Economic Behavior* reports that subjects seem to use different parts of their brains when they consider financial gains and when they consider financial losses; more recently, they have found that subjects use different parts again to evaluate the magnitude and probability of those gains and losses. Knutson and Peterson's work is part of an increasing effort to figure out how economic utility may be coded quantitatively in various regions of the brain. If economists could track the different components of utility in a statistical way, they could understand why some people take risks and some don't—and possibly predict their future behavior.

Protect Us from Ourselves

Suppose that the science and technology of neuroeconomics progress according to plan. (They won't, of course, but let's set that aside for now.) At some point in the future, our brains' inner workings, our innermost thoughts, all of our decision-making processes, could be deciphered and displayed individually and unambiguously, like the hands of poker players in televised tournaments. What would we do with this information? How would we protect ourselves? Entire industries—finance, health care, advertising—stand to flourish or die based on the answers.

Let's consider some early indications of what the social consequences of neuroeconomics could be. In finance, an initial attempt at using brain studies to model markets was put forth in a recent paper by the economist Andrew Lo. Lo, the director of MIT's Laboratory for Financial Engineering, argues that the standard theory of "efficient markets"—which assumes investors have perfect information and behave rationally—should be replaced by an "adaptive markets" hypothesis that accounts for psychological factors and responses. He is currently working to formalize the hypothesis mathematically and to implement predictive models of equity risk premium and other stock-market returns using high-performance parallel processors.

Lo is perhaps best known for a study published in 2002 in which he and Dmitry Repin of Boston University used a polygraph-like system to measure the physiological responses of securities traders as they did their jobs; the researchers concluded that emotions like anxiety and fear play a large role in financial decision-making, and that they may have more influence on less experienced workers than on seasoned veterans. "Within five years, neuroeconomics will become mainstream," says Lo. "In 15 to 20 years, it will be fully accepted."

Well before then, expect to see the influence of "neuromarketing" on advertising. Recent experiments have imaged people's brains as they chose between brand names, even movie trailers. Researchers believe that by recording which brain areas are activated during choices, they are starting to be able to predict preferences based on brain scans alone. Some marketing experts believe such research could be used to supplement product surveys and might, eventually, indicate how to ignite pleasurable feelings in consumers at the prospect of rewards.

All of this raises questions about privacy and individual autonomy—and how society might wish to regulate much more effective advertising. "As corporations learn to take further advantage of our weaknesses, we may soon be asking for government to take on the role of protector and guarantor of our privacy, happiness, and savings," says Peterson, who is a managing partner of San Francisco firm Market Psychology Consulting.

That may sound a little excessive. But neuroeconomists are thinking about the influence their work could have on public policy. One of the earliest neuroeconomics papers to address policy implications, "Addiction and Cue-Triggered Decision Processes," by Stanford economists Douglas Bernheim and Antonio Rangel, makes some sensible recommendations. The researchers propose a mathematical theory of addiction (essentially, an economic model) that takes into account findings from brain scans of recovering addicts and physiological measurements from the reward pathways of animal brains. The theory provides a way to determine, for instance, the probability that a recovering alcoholic will drink, depending on the placement of beer cans in a supermarket. It also predicts the effects of addictive-substance policies on the welfare of addicts and casual users—which could be used to compare the socioeconomic consequences of, say, raising taxes on alcohol or subsidizing rehabilitation programs. According to Rangel, this kind of analysis might also apply to other behaviors, like compulsive shopping. The hope is that such models, grounded in the latest neurobiological thinking, will better inform policymakers and lead to more intelligent legislation.

Neuroeconomics seems to be a promising step toward a more unified theory of human behavior. Indeed, by opening up the brain and studying how its circuits produce economic decisions, scientists may provide answers to some of the questions debated by philosophers for centuries. Why do we make the choices we make? And why is it so hard to figure out what we really want? ■

Gregory T. Huang is senior writer at Technology Review.

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How the Fed Learned to Love Technology

Greenspan avoided the mistakes of his Federal Reserve predecessor.

BY ROGER LOWENSTEIN

When Alan Greenspan retires in January, after eighteen and a half years as chairman of the Federal Reserve Board, he will have served longer than any previous occupant save William McChesney Martin Jr., who held the job for nearly 19 years. A lot happened during the Greenspan era—two wars in the Persian Gulf, various currency crises, three stock market meltdowns—but no topic interested him as much as the revolution in information technology.

Greenspan will ever be associated with the bubble in high-tech stocks—first for warning, in 1996, that investors might be succumbing to "irrational exuberance," and later, after stock prices had soared and investors truly had succumbed, for presiding over the collapse. Greenspan's critics tend to focus on his enthusiasm for Silicon Valley before the crash; his defenders point out that, after all, the stock market has begun to recover. Both points are somewhat tangential to his real legacy. Greenspan's primary interest was never the precise level of tech-stock prices: it was how the computer was transforming American society.

"Virtually unimaginable a half-century ago was the extent to which concepts and ideas would substitute for physical resources and human brawn in the production of goods and services," he told an audience in 1996. At that time, the chairman drew comparisons between the computers of our day and the innovations of earlier eras. Four years later, Greenspan was advancing the proposition that our era was indeed different. "When we look back," he said on January 13, 2000, "we may conceivably conclude...that...the American economy was experiencing a once-in-a-century acceleration of innovation...[and] it is information technology that defines this special period."

In August 1987, when Greenspan took the reins at the Fed, information technology was still relatively young. Mainframe computers had long been a staple of American industry, of course, but most Americans did not yet own PCs, and as Greenspan was to observe, "the billions of dollars that businesses had poured into" computer technology "seemed to leave little imprint on the overall economy." The Internet as we know it did not exist. And oh, yes, the Nasdaq was barely above 400. Greenspan, of course, had nothing to do with creating technology, but as a central banker he allowed technology to influence economic policy to an astonishing degree. Did he get the big picture right?

Peculiar Punch

The proper duty of the Fed chief was forever defined by Martin, who served from 1951 to 1970, as to "take away the punch bowl just as the party got going." Thanks to Robert Bremner's new biography *Chairman of the Fed: William McChesney Martin Jr. and the Creation of the American Financial System*, we have a deeper understanding of how complex this job can be. Greenspan isn't mentioned in the book, but his shadow hangs over it. Between them, Martin and Greenspan dominated central banking for half a century—a period that saw the U.S. economy reassert itself after the calamity of the Depression; fall siege, during the 1970s, to the worst bout of inflation in recent history; and then recoup in the great boom of the 1990s. Bremner's book, on bookstore shelves during Greenspan's last year in office, stirs us to an uncomfortable contrast. How are we to reconcile the failure of the puritanical Martin with the success of Greenspan, who can be accused not only of failing to remove the punch bowl, but also of spiking the punch?

Greenspan's infatuation with the peculiar punch being ladled out in Silicon Valley is a matter of record. To cite but one example, in April 2000, when dot-com fever was at its peak, he spoke at the White House Conference on the New Economy and warmly referred to the "prescience" of security analysts who were then touting tech stocks at lunatic prices. "There are many who argue, of course, that it is not prescience but wishful thinking," Greenspan acknowledged. "History will judge."

The Other Famous Fed Chief

Chairman of the Fed: William McChesney Martin Jr. and the Creation of the American Financial System
By Robert P. Bremner
Yale University Press, 2004, $38.00

William McChesney Martin Jr. was chief of the Federal Reserve from 1951 to 1970.

History did judge. The bubble popped, and yet the fact is that Greenspan's overall record is one of price stability and robust growth, dampened by a pair of only mild recessions. Meanwhile, the humorless Martin, who essentially equated speculation with sin, somehow managed to let inflation careen out of control.

Both men entered office as orthodox inflation hawks, and both eventually adopted more-nuanced—one might say more-relaxed—views toward restraining prices. Aside from a shared passion for tennis, however, that is where the similarities ended. The straitlaced Martin, born in 1906, learned macroeconomics from firsthand experience, much of it painful. His grandfather lost his grain business to the depression of 1893, and Martin spent his early career, as a broker and then as a reformist president of the scandal-ridden New York Stock Exchange, trying to emerge from the suffusing gloom of the Great Depression. Contrariwise, Greenspan's education was intellectual and faintly bohemian: the conservative economist, who grew up in Washington Heights in Manhattan and studied at the Juilliard School of Music, emerged from Ayn Rand's salon and, improbably, the swing band in which he blew his clarinet.

A Bumpy Ride

As Fed chief, Martin patiently worked to free the central bank from executive control in the aftermath of World War II and to reassert a system of market rates. His reward was to have President Truman label him a "traitor."

Martin also had difficulties with President Kennedy. The economy had grown sluggishly under Eisenhower, and Kennedy was anxious to energize it. He adopted a Keynesian prescription: tax cuts and deficit spending. This was the same tonic President George W. Bush would later adopt. Martin, though, worried about deficits. As a central banker, he frowned on the idea that "a little bit" of inflation could be benign. "There is no validity," Martin countered, to the notion "that any inflation, once accepted, can be confined to moderate proportions." This would prove more prophetic than even Martin feared.

Under Lyndon Johnson, domestic spending soared, just as the United States became deeply involved in Vietnam. Martin correctly sensed that LBJ was underaccounting for the war's cost. He fretted to LBJ that the United States was "heading toward an inflationary mess," and despite LBJ's pleading, in December 1965 the Fed raised rates, decisively. Then, after having fought off LBJ, Martin inexplicably crumbled. He felt committed to the administration, and he perceptibly—and tragically—shifted his emphasis from managing interest rates to working on the president to balance the budget.

In retrospect, he missed, or underestimated, the salient trend of his era. It wasn't budget deficits (though they were real) but incipient inflation. By the time Martin retired in 1970, prices were rising at a 6 percent annual clip. Inflation would exceed 13 percent before Paul Volcker, appointed in 1979, brought it down. When Greenspan began his first term as chairman, inflation was 4 percent; clearly, he does not deserve the credit for taming it. But it would be a while before markets realized the dragon had been slain. And just as Martin had to flout public opinion in the 1950s, tightening monetary policy despite fears that a new depression lurked around the corner, so Greenspan had to break with the postinflationary mindset. The New Economy was his ticket.

As a Wall Street economist, Greenspan was well positioned to recognize technology's impact. Wall Street, which in the 1970s had nearly drowned in the physical paper brokers generated, was one of the first industries to productively use computers. Not only did they speed trading, but they made new forms of trading, and new financial instruments, possible. To Greenspan and others, it appeared that technology would break down barriers, promote competition, and lessen the need for regulation. "New technology," he noted, "has fostered mergers that allow firms to take great advantage of economies of scale and thus reduce costs."

Greenspan was perhaps too infatuated with technology to appreciate its potential for mischief. He was consistently, and inexcusably, lax in pressing for rules that would govern the new finance. And if technology had led *only* to mischief, he would have been a failure. But of course, technology has mainly been a blessing, not least for allowing firms to make more of their resources. Greenspan sensed *that* far earlier than almost anyone.

The pivotal moment came in September 1996. The economy was picking up steam, and labor markets were tight. According to conventional analysts, businesses would be forced to pay more for labor and to pass on their costs as price hikes. Preventing inflation, the argument went, meant raising interest rates. But inflation was falling. Greenspan saw that "something else might be going on," recalls then Fed governor Alice Rivlin. His hypothesis was that IT investments were making businesses more productive. If so, pay raises wouldn't really be "raises": workers would simply be receiving greater compensation for greater output.

And yet, even though business had been pouring money into computers for years, the official data indicated that the rate of productivity growth remained low. "Why have our recent productivity data failed to register any improvement?" Greenspan asked in a speech. "Is it possible that much of the frenetic activity [involving computers] is mere wheel spinning, and as a consequence, very little real value added is being produced—or maybe ever will be?" Greenspan didn't think so. A majority of the Fed's governors wanted to nip the inflationary threat, even before it was visible, by raising rates, but Greenspan insisted that rates remain stable. The boom continued for four more years. This had profound social consequences, as it was only after 1996 that real wage increases began to dribble down to middle- and lower-income workers. Nonetheless, inflation remained quiescent, and sharply higher productivity was soon visible in the official stats. Greenspan's bet had nothing to with dot-com stocks; he thought technology was making the rest of the economy—steel, finance, retail—more efficient. And so it was.

He was wrong about tech stocks, and his endorsement of the Bush deficit may turn out to be grievously wrong. But Fed chiefs, ultimately, are paid neither to pick stocks nor to balance budgets. As Martin understood, the central banker has two primary tasks: maintain stable prices and promote growth. Alas, the banker who famously stood watch over the punch did not fare as well as the musician with an ear for the pulse of computers. ■

Roger Lowenstein's most recent book is Origins of the Crash: The Great Bubble and Its Undoing.

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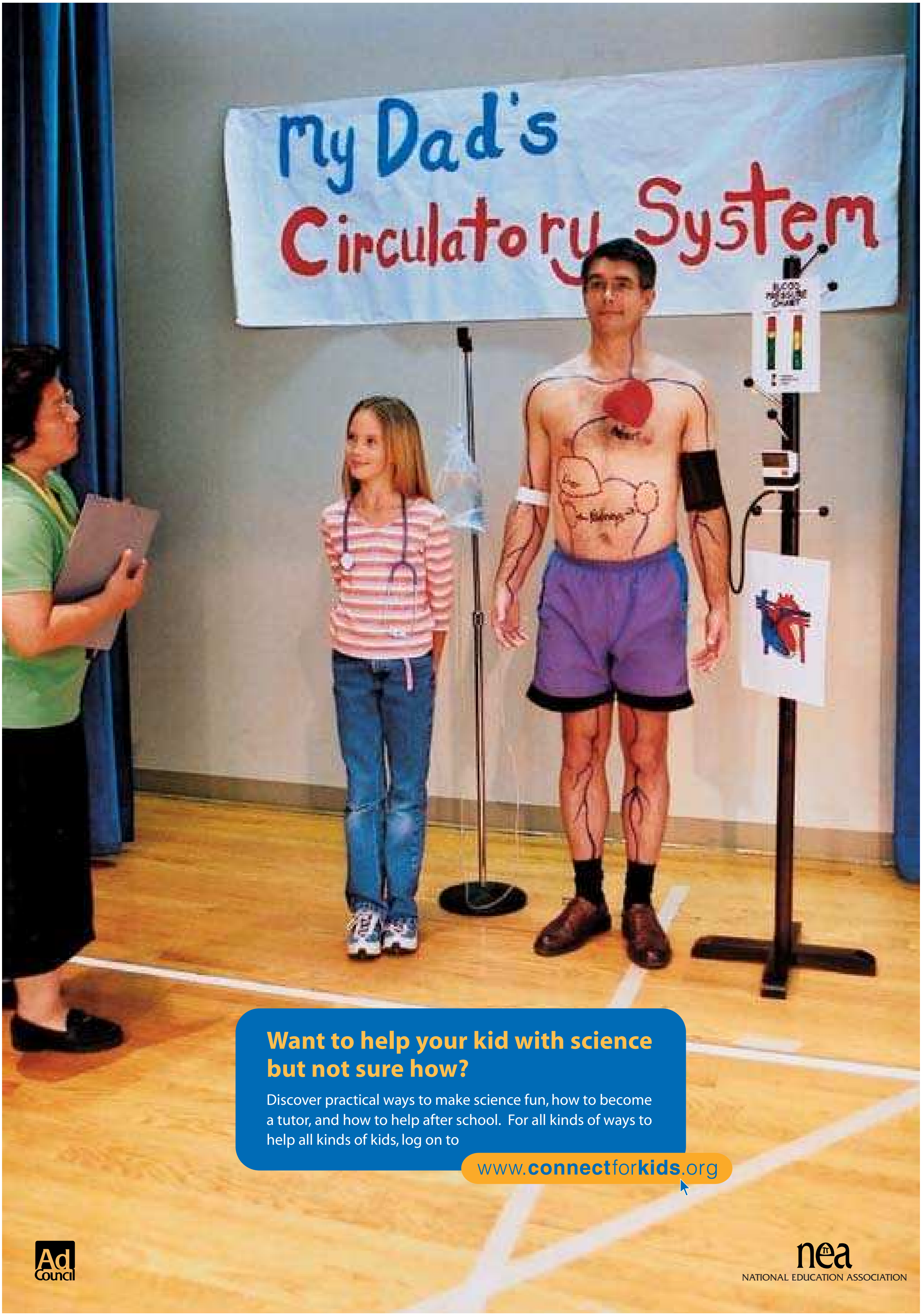
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Reviews

Greenhouse Gas

Michael Crichton's new novel fingers the wrong villains in global warming.

BY JOSEPH ROMM

Not a Cloud in the Sky
State of Fear
By Michael Crichton
HarperCollins, 2004, $27.95

MICHAEL CRICHTON HAS written that rarest of books, an intellectually dishonest novel. Crichton has made a fortune exploiting the public's fears: *Prey* (fear of nanotechnology), *Rising Sun* (fear of Japanese technological supremacy), and *Jurassic Park* (fear of biotechnology). These books attack the hubris of those who use technology without wisdom. In *Prey*, he warns, "The total system we call the biosphere is so complicated that we cannot know in advance the consequences of anything that we do." Given the author's past, one might expect that a Crichton book on global warming would warn about the risk of catastrophic climate change—the unintended consequences of humanity's reckless, irreversible experiment on the biosphere.

But *State of Fear* takes the reverse view. Crichton argues that the environmental and scientific communities have fabricated the threat. He wants readers to fear those who argue that climate change is real, caused by human technologies, and dangerous. In the novel, a mainstream environmental group plots to create extreme weather events that will cause the deaths of thousands of people in order to trick the public into accepting global warming as truth. They try to create a killer seismic tsunami timed to coincide with a conference on abrupt climate change. That's a major mistake by Crichton: seismic tsunamis aren't caused by global warming, as any climate scientist, even an evil one, knows.

Because the evidence for–and scientific consensus on–the human causes of climate change is now so strong, Crichton cannot make his case simply on the evidence. Instead, he must distort the facts and accuse the scientific community of bad faith in order to make his case. And he does so, repeatedly.

Crichton portrays environmentalists as uninformed, hypocritical, or simply evil. He creates a scientist-hero, John Kenner, to save the day. (For added credibility, Kenner is an MIT professor—though he sounds more like Rush Limbaugh than any MIT faculty member I've met.) Speaking through Kenner, Crichton makes a faulty case against the environmentalists. Kenner says, for instance, that a real NASA climatologist, James Hansen, has been discredited for overestimating the impact of global warming "by three hundred percent" during 1988 testimony in Congress. In fact, Hansen's prediction was very close to accurate. The smear Crichton cites was created 10 years later, when global-warming skeptic Patrick Michaels misrepresented the testimony.

Crichton also strains to discredit global-warming fears by presenting them as faddish. He has one environmentalist say (incorrectly), "in the 1970s, all the climate scientists believed an ice age was coming." Global warming did level off between 1940 and 1975. We now know that this was largely a result of dust and aerosols sent by humans into the atmosphere that temporarily overwhelmed the warming effect from greenhouse gases. In the 1970s, it was not yet clear whether the cooling effect from aerosols would be greater than the heating produced from greenhouse gases. Now we know: the heating wins. This episode, fairly explained, would give readers greater confidence in our understanding of climate science, not less.

The dissembling even leaks into the book's bibliography, where Crichton mischaracterizes the landmark 2002 National Research Council report *Abrupt Climate Change*: "The text concludes that abrupt climate change might occur sometime in the future, triggered by mechanisms not yet understood." The report actually concludes, "Abrupt climate changes were especially common when the climate system was being forced to change most rapidly. Thus, greenhouse warming...may increase the possibility of large, abrupt, and unwelcome regional or global climatic events." *State of Fear* is riddled with such misinformation. For a thorough debunking, go to www.realclimate.org, a site that gives the lie to Crichton's scurrilous claim that in climate science "open and frank discussion of the data, and of the issues, is being suppressed." Sadly, Crichton smears the work of countless scientists who are trying to predict and prevent the unintended consequences of technological hubris. ■

Joseph Romm, an MIT-trained physicist, was acting assistant secretary of energy during the Clinton administration. His latest book is The Hype about Hydrogen: Fact and Fiction in the Race to Save the Climate, *which was selected by* Library Journal *as one of the best science and technology books of 2004.*

From the Lab

EDITED BY MONYA BAKER

Each month brings new investigative tools, new ideas for revolutionary technology, and revolutionary applications of existing technology. No one can know today which will matter most tomorrow. But these represent *Technology Review*'s best prediction.

INFORMATION TECHNOLOGY

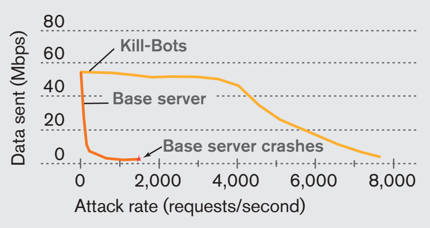
Kill the Bots!

Software thwarts malicious hackers

CONTEXT: The malicious computer programs known as "worms" infect more than 30,000 new computers every day. Unbeknownst to their owners, the compromised machines follow orders to send spam, say, or to access particular websites. If enough of these so-called zombie machines simultaneously contact a particular Web server, they can knock it out of commission. Professional hackers have used the threat of such "distributed denial-of-service attacks" to extort money from businesses. Last year, one company's business manager was indicted for paying hackers to use zombies to take down competitors' websites. The zombies dodge a Web server's defenses by disguising themselves as legitimate users and then block access to the server by overloading not only its network bandwidth, but also its CPU, memory, disk space, and database resources. Now, led by Dina Katabi, researchers from MIT, Princeton University, and Akamai Technologies have developed Kill-Bots, a clever, simple, and cheap means of distinguishing friend from foe. Unlike other products, it allocates a server's system resources only after a user is confirmed as legitimate.

Protect Your Server

A Kill-Bots Web server kept pace until it received 4,000 requests per second; the unprotected base server slowed to a crawl at 200.



METHODS AND RESULTS: Kill-Bots, a software modification to a server's operating system, kicks in whenever a website is in danger of being overwhelmed by traffic. The software asks requesters to solve a simple graphical puzzle before it grants access to server resources like buffer space. Humans can solve these puzzles easily; zombies cannot do so at all. Addresses that repeatedly request site access without solving the puzzle are blacklisted automatically. When the load on the Web server decreases, it stops issuing puzzles and accepts requests from nonblacklisted addresses, so even real users who did not solve the puzzle can gain access.

In experiments, a Kill-Bots-protected Web server successfully endured five times as many hits as an unprotected Web server. Not only did the Web server stay online, but protected websites also maintained speedy response times, even during the height of the attack.

WHY IT MATTERS: Worries over distributed denial-of-service attacks are spreading. Most Web server defenses use authentication procedures that are easily outwitted and depend on replicated content, multiple CPUs, and extra bandwidth, all of which cost money. Kill-Bots is much cheaper and can be easily deployed; it requires no changes in users' Web browsers and works with the very large number of Web servers running Linux. Although Kill-Bots occasionally misclassifies legitimate users as zombies, it allows websites under attack to remain available and so promises to keep the Web open for business, while barring the way for thieves and vandals.

Source: Kandula, S., et al. 2005. Botz-4-Sale: surviving organized DDoS attacks that mimic flash crowds. Paper presented at 2nd Symposium on Networked Systems Design and Implementation. May 2–4. Boston, MA.

Dethroning the Transistor

A new molecular logic switch

CONTEXT: The terms "semiconductor" and "computer" have become entwined; better semiconductor manufacturing has enabled the release of chips with smaller and faster circuits every year. But in a decade, the miniaturization of silicon transistors may reach physical limits that prevent further improvements. So engineers from Hewlett-Packard have created a molecular device that could be the heart of the computer of the future.

METHODS AND RESULTS: The circuits proposed by Phil Kuekes and his HP colleagues rely on a "crossbar": an array of crossed metal wires separated by a single layer of molecules. Like a transistor, a crossbar can be switched between a high and low conducting state, allowing it to store information. Kuekes shows how to link crossbars so that they can not only store data but also restore noisy data and apply a logic operation called inversion, which swaps binary *0*s for *1*s and *1*s for *0*s. The crossbars can be linked with other components to generate the entire family of logic needed for computing. The researchers have yet to combine all these capabilities into a stand-alone computing device, and they have not yet found a way to make molecular junctions that switch states quickly and reliably enough to compete with silicon transistors. Nonetheless, they have provided the first demonstration that crossbars can perform all the functions transistors can perform.

WHY IT MATTERS: The HP researchers have cleared a path toward a computer chip without conventional transistors. The process used to create their crossbars is inexpensive and in principle could lead to logic elements even smaller than those constructed from the most advanced silicon transistors, which would enable faster and more efficient computer chips. But even if the performance and reliability of crossbars surpass those of transistors, they may still lack the muscle to compete with the entrenched semiconductor industry. Crossbars may instead find their first applications elsewhere, in flexible logic devices, for example, or displays.

Source: Kuekes, P. J., D. R. Stewart, and R. S. Williams. 2005. The crossbar latch: logic value storage, restoration, and inversion in crossbar circuits. *Journal of Applied Physics* 97:034301.

Brighter Silicon

Toward more-efficient optical devices

CONTEXT: Silicon is good at shuttling electrons around chips but much worse than most other semiconductors at manipulating light. This shortcoming has kept optical chips, which transmit information more efficiently than electrical chips, from wider use. Silicon "nanocrystals," a few atoms of silicon covered with an oxide layer, emit light more efficiently than bulk silicon, but devices incorporating them wear out quickly and are still too inefficient for most applications. Now, a team led by Harry Atwater of Caltech has improved silicon's ability to emit light, giving a boost to an industry looking for new ways to make faster chips.

METHODS AND RESULTS: In a conventional light-emitting diode (LED), electrons traveling through a semiconducting crystal meet electron "holes"—or gaps left in the crystal by absent electrons—and lose energy, which is emitted as light. But this approach doesn't work well with silicon nanocrystal LEDs, where electrons moving toward the holes can collide with atoms in the crystal and displace them, degrading performance.

Previous silicon LEDs used separate electrodes to inject holes and electrons into silicon nanocrystals. But Atwater and colleagues figured out how to inject both from a single electrode. In their device, a thin layer of silicon nanocrystals sits atop an electrode that alternates between adding electrons and adding holes. This keeps electrons from rocketing violently across the crystal and damaging it. Also, by eliminating one of the entry and exit points for electrons, the Caltech group has made devices that are easier to fabricate and more consistent in performance.

WHY IT MATTERS: The new LED can be built using standard equipment that could be integrated into a chip-manufacturing line. Its performance, however, is still low enough to limit its use. To improve the processing speed of silicon chips, the LED would have to switch on and off more quickly; to be of use in a display, it would have to consume less power. Nonetheless, the semiconductor industry has much practice improving the performance of silicon chips. The problems of speed and power may not remain unsolved for long.

Source: Walters, R. J., G. I. Bourianoff, and H. A. Atwater. 2005. Field-effect electroluminescence in silicon nanocrystals. *Nature Materials* 4:143–146.

BIOTECHNOLOGY

Knocking Out Malaria?

Genetically engineered vaccine shows promise

CONTEXT: The world's first vaccines were made from weak forms of disease-causing microbes. A more modern approach is to instead use one or a few of a microbe's signature molecules. But the malaria parasite—*Plasmodium*—foils this strategy because at different developmental stages it has different surface proteins. However, the older approach also poses problems: insufficiently weakened parasites might bring on the disease, but overly weakened ones are ineffective. Researchers led by Kai Matuschewski at the Heidelberg University School of Medicine in Germany and Stefan Kappe at the Seattle Biomedical Research Institute have announced a promising mixture of new and old. They have, for the first time, made a malaria vaccine by weakening the parasite through genetic engineering.

METHODS AND RESULTS: *Plasmodium* constantly changes both appearance and address, moving from mosquitoes' guts to their salivary glands to mammals' liver cells to their blood. With the newly sequenced *Plasmodium* genome as a guide, the researchers looked for genes the parasite needs to move from liver to blood. They found such a gene and completely deleted it from the version of *Plasmodium* that infects rodents. Then, they injected rats and mice with the genetically modified parasites. None got malaria. Two months after vaccination, the rodents were injected with 50,000 nonmodified parasites (the equivalent of hundreds of bites from infected mosquitoes). Encouragingly, none got sick.

WHY IT MATTERS: Malaria kills millions annually; the sickness stifles development in afflicted countries by keeping people from work and school and by draining health resources. The vaccine developed by Matuschewski and colleagues must still show that it is able to prevent disease

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in humans and for the long term. In mice, the vaccine must be administered two or three times, delivering thousands of parasites that can be grown only in mosquitoes' salivary glands. To save lives, future whole-parasite vaccines must be more potent and easier to produce. Or perhaps knowledge gleaned from genetically modified vaccines will inspire more successful versions of other vaccines. If either happens, this devastating disease could be eradicated within a generation.

Source: Mueller, A. K., et al. 2005. Genetically modified *Plasmodium* parasites as a protective experimental malaria vaccine. *Nature* 433:164–7.

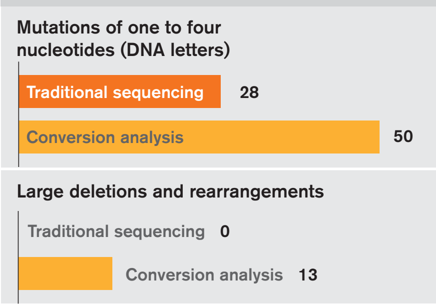
Seeing Missing Letters

Genetic test promises more accurate diagnoses

CONTEXT: There are many ways that a gene can go wrong. A single DNA "letter," or nucleotide, in a sequence of letters may be replaced with another. Or a long string of letters may get deleted, reversed, or duplicated. With certain diseases, patients are likely to have mutated versions of the same gene but unlikely to have the same mutation. Current genetic tests overlook certain kinds of mutations; they are a bit like a word-processing program that can find misspelled words but not missing words or sentences. They usually sequence a gene's DNA in separate chunks, examining each chunk for mutations. But people have two copies of almost every gene, and if a chunk is entirely missing from one copy, current tests will detect the intact chunk from the other copy. To find out how many mutations conventional tests miss and so determine how useful new genetic tests could be, Graham Casey of the Cleveland Clinic and colleagues separated copies of genes to look at each individually.

New Gene Test

Conversion analysis detected harmful mutations that traditional sequencing did not.



METHODS AND RESULTS: The researchers studied cells from 89 colon cancer patients, each of whom appeared to have a mutation in one of three genes. They examined the cells' DNA using both traditional sequencing and another technique called "conversion analysis." In conversion analysis, researchers create new cells, each of which contains only one copy of the gene being studied; they then compare the RNA messages coming from both copies.

Sequencing analysis found 28 mutations deemed likely to have ill effects; conversion analysis found all these and 14 more. Sequencing also found 42 mutations that could not be classified as either harmful or harmless; conversion analysis identified 21 of these as harmful (and the rest as innocuous). Thus, traditional sequencing identified 28 harmful mutations, while conversion analysis found 63.

WHY IT MATTERS: Genetic deletions likely contribute to breast cancer, neurofibromatosis, Duchenne's disease, and Parkinson's. Researchers and physicians know that traditional tests do not detect large genetic deletions. As a result, doctors often advise preventive procedures to at-risk patients, no matter what the genetic tests say. Not only may patients be unnecessarily worried, but they may also undergo expensive and painful procedures, like colonoscopies, that are unlikely to benefit them. Even healthy patients cannot know how likely they are to pass genetic mutations to their children. Casey and colleagues have, for the first time, rigorously examined how frequently such mutations are missed and shown that, for some diseases, the more difficult genetic tests might be worth the investment.

Source: Casey, G., et al. 2005. Conversion analysis for mutation detection in MLH1 and MSH2 in patients with colorectal cancer. *Journal of the American Medical Association* 293:799–809.

Beaming Biodata

Mutation detection goes wireless

CONTEXT: DNA chips for detecting genetic variations abound. Typically, a processed biological sample is placed on a chip, which then must be loaded into a separate, expensive device for reading. Now, Yoshiaki Yazawa and colleagues at Hitachi have designed a tiny chip that not only detects DNA variation but can report it wirelessly from the inside of a sealed sample container. These chips could be dropped directly into a solution containing copies of patient DNA and should be cheap enough to be disposable.

METHODS AND RESULTS: The chip packs a biosensor, radio transceiver, and antenna coil onto 2.5 by 2.5 millimeters of silicon. An off-the-shelf external unit powers the chip with radio waves and reads its transmissions. To detect a particular DNA sequence, researchers add the complementary sequence to the sample along with the chip. If DNA in the sample binds to the probe sequence, an enzyme emits light. When the sensor on the chip detects the change in light, the radio unit sends a signal to the external unit.

This is a simpler technique than the one used by most other chips, which requires fluorescent dyes, lasers, and microscopes. Additional chips can be added to the sample to boost accuracy or to detect different kinds of variations. Hitachi researchers believe that up to 100 variations could be measured at one time. Also in development are wireless sensors that use the same technology to monitor temperature and pH, which could enable better control of experimental conditions and thus more reliable readings.

WHY IT MATTERS: DNA analysis promises to make medicines more effective, if it can be made easy and cheap enough. Hitachi's chip is the first that can both detect mutations (albeit so far only the simplest and most common kind) and report them wirelessly. Since this kind of chip can transmit data from inside a sealed con-

tainer, samples tested with it are less likely to be contaminated by researchers or the environment, and samples containing pathogens are less likely to infect workers. Assuming patient samples can be prepared easily for chip analysis, the chip could also make it easier to detect DNA variations in settings less controlled than a research lab. Though the research is still in its initial phases, Hitachi expects that the chips could be used in clinics or small hospitals to help doctors decide which drugs to prescribe for patients.

Source: Yazawa, Y., et al. 2005. A wireless biosensing chip for DNA detection. Paper presented at 2005 IEEE International Solid-State Circuits Conference. Feb. 6–10. San Francisco, CA.

Xenotransplant

Pig hearts in humans?

CONTEXT: When he was a heart surgeon, David Cooper would have 140 patients referred to him for transplants each year; because of the shortage of donor organs, only about 25 would receive them. Now an academic researcher at the University of Pittsburgh Medical Center, Cooper is part of a broad effort to search for ways to use pig organs for human transplants.

Without extremely high levels of immunosuppressive drugs, pig organs seldom last for half an hour in, say, baboons. The organs swell up and turn black and must be removed quickly, or the animals may die. Cooper led a team of scientists from Harvard Medical School and Immerge Biotherapeutics in determining what would happen when hearts from pigs genetically modified to seem less "piglike" to a foreign immune system were transplanted into baboons.

METHODS AND RESULTS: The baboon's immune system targets the pig organs for attack mainly because of a particular sugar that covers porcine blood vessels. Three years ago, scientists created pigs unable to make this sugar by deleting a gene for a certain enzyme. Cooper's team transplanted hearts from the genetically modified pigs onto the abdomens of eight baboons, where the researchers could tell how strongly the pig hearts were beating. Three baboons died for reasons other than organ rejection, and the hearts remained viable. In the other five baboons, the hearts stopped beating between 59 and 179 days after transplantation, at which time they were surgically removed. The small blood vessels in the organs were full of tiny clots, probably caused by a mismatch between tissues and blood-clotting systems. But the researchers found evidence that this clotting process can be at least slowed with anticlotting medicines, like aspirin. None of the baboons suffered serious infections as part of the study.

WHY IT MATTERS: Cooper and colleagues' study marks the first transplant using pigs engineered to lack a gene and the first time xenotransplanted organs have survived for months when immunosuppressive drugs were administered in doses similar to those used in humans. It also marks the longest time a pig heart has survived in another species. In previous work, organ rejection has been inhibited, though not as dramatically, by using pigs engineered to contain human genes that protect their organs from the human immune system. Experiments using additional pigs with these human genes and without the pig sugar gene are planned, but the first pig-to-human transplants are years away, says Cooper. First, xenotransplants must be deemed as likely to help patients as other available treatments, like mechanical heart-assistive devices. Even then, concerns about ethics and infectious disease must be addressed.

Source: Kuwaki, K., et al. 2005. Heart transplantation in baboons using α1,3-galactosyltransferase gene-knockout pigs as donors: initial experience. *Nature Medicine* 11:29–31.

NANOTECHNOLOGY

Nanomovies

An atomically sharp device records motion

CONTEXT: To build useful small devices, engineers must be able to see what they are doing, so they use atomic force microscopes to take pictures with nanometer resolution. To create images, the microscopes move a sharp tip across the surfaces of such tiny objects as silicon transistors or DNA molecules. The tip, just a few atoms across, moves slowly: at best, commercial atomic force microscopes can take only about one image every ten seconds. So they're not much use in studying fast processes. Now, researchers at MIT have found a way to capture nanoscale images a million times faster.

METHODS AND RESULTS: The technique developed by Mekhail Anwar and Itay Rousso yields high-speed movies of processes that repeat regularly. An object to be imaged is set in motion, and the tip captures information about surface height at one location only. Once enough data is collected, the tip moves a few nanometers to its next location, and the process is repeated. Each location thus becomes a pixel in a motion picture, and aligning the pixels in time produces a time-lapse movie of the process.

Unconstrained by the rate at which it can move forward, the tip collects data as quickly as its up-and-down movements can be recorded. Anwar and Rousso demonstrated the potential of their technique by imaging the motion of a microdevice with a time resolution of five microseconds.

WHY IT MATTERS: Because they scan slowly, atomic force microscopes are now used only to take snapshots of surfaces. Atomic force movies could help researchers analyze the motions of the microfluidic pumps used in the purification and analysis of DNA and proteins or provide moving images of biological processes.

Since any atomic force microscope could, in theory, be programmed to produce such movies, academic and industrial researchers have the means, motive, and opportunity to try the technique. Thus, nano moviemaking could become an important way to help researchers see what molecular devices are doing, analyze their performance, and determine how to improve them.

Source: Anwar, M., and I. Rousso. 2005. Atomic force microscopy with time resolution of microseconds. *Applied Physics Letters* 86:014101.

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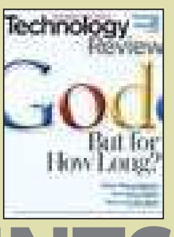

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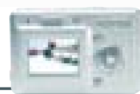
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Father of Prozac Nation

Julius Axelrod's research helped launch the multibillion-dollar antidepressant market

BY ANDREW P. MADDEN

Julius Axelrod, a pharmacologist and neuroscientist who shared the 1970 Nobel Prize in medicine for his insights into how human brain cells communicate with each other, died last December 29 at the age of 92. Axelrod's findings about the behavior of neurotransmitters—the chemical messengers of the brain—drew a clear connection between the physiology of the brain and emotional moods. His discoveries paved the way for the multibillion-dollar antidepressant drug industry, and in so doing helped give rise to what was later called by some "Prozac Nation."

Axelrod, who was known as "Julie," focused on how the neurotransmitters secreted by a brain cell travel across a synapse (the space between nerves) and are then picked up by a receptor on the surface of another cell. Before Axelrod's research in the late 1950s, scientists believed that neurotransmitters were broken down by enzymes in the brain after they crossed a synapse. But Axelrod's findings suggested that, instead, they were retrieved by the very cells that released them, in a process called "reuptake."

The identification of this process allowed drug researchers to pinpoint areas where they might boost or lower chemical levels in the nervous system. For example, selective serotonin reuptake inhibitors, the class of antidepressants that includes Prozac, work by blocking the reuptake process that Axelrod identified.

Born on Manhattan's Lower East Side in 1912, Axelrod was the first to describe his origins as humble, even inauspicious. The son of a Jewish basket maker who emigrated from Polish Galicia, Axelrod fortified his undistinguished early education by spending most of his time at the library reading Upton Sinclair, H. L. Mencken, and Leo Tolstoy.

After attending New York University for one year, Axelrod ran out of money, which forced him to transfer to City College of New York. Although he showed a greater aptitude for history, philosophy, and literature, he decided to apply to medical school; but he was rejected everywhere. He completed his undergraduate studies in 1933 at the height of the Depression and managed to find a job paying $25 a month at an NYU lab.

Axelrod soon took a research job at the New York City Department of Health's Laboratory of Industrial Hygiene, where he remained until 1946, taking night classes and earning a master's in chemistry along the way. In 1949, he joined the National Heart Institute and briefly returned to school in 1954 to earn his PhD from George Washington University.

In 1955, Axelrod joined the National Institute of Mental Health (NIMH), where he established his famed laboratory. He remained at NIMH until his retirement in 1984 and presided over a cadre of postdoctoral students, many of whom would become distinguished researchers themselves. He also became a vocal advocate for the preservation of basic research in the sciences and took up various political causes.

Axelrod was happiest, however, away from the spotlight, acknowledging his accomplishments with modesty and even a touch of self-deprecation. As he liked to recount, he was notified of his Nobel Prize while on his annual trip to the dentist. He was speechless, he said, but only because his mouth was stuffed with cotton. ■

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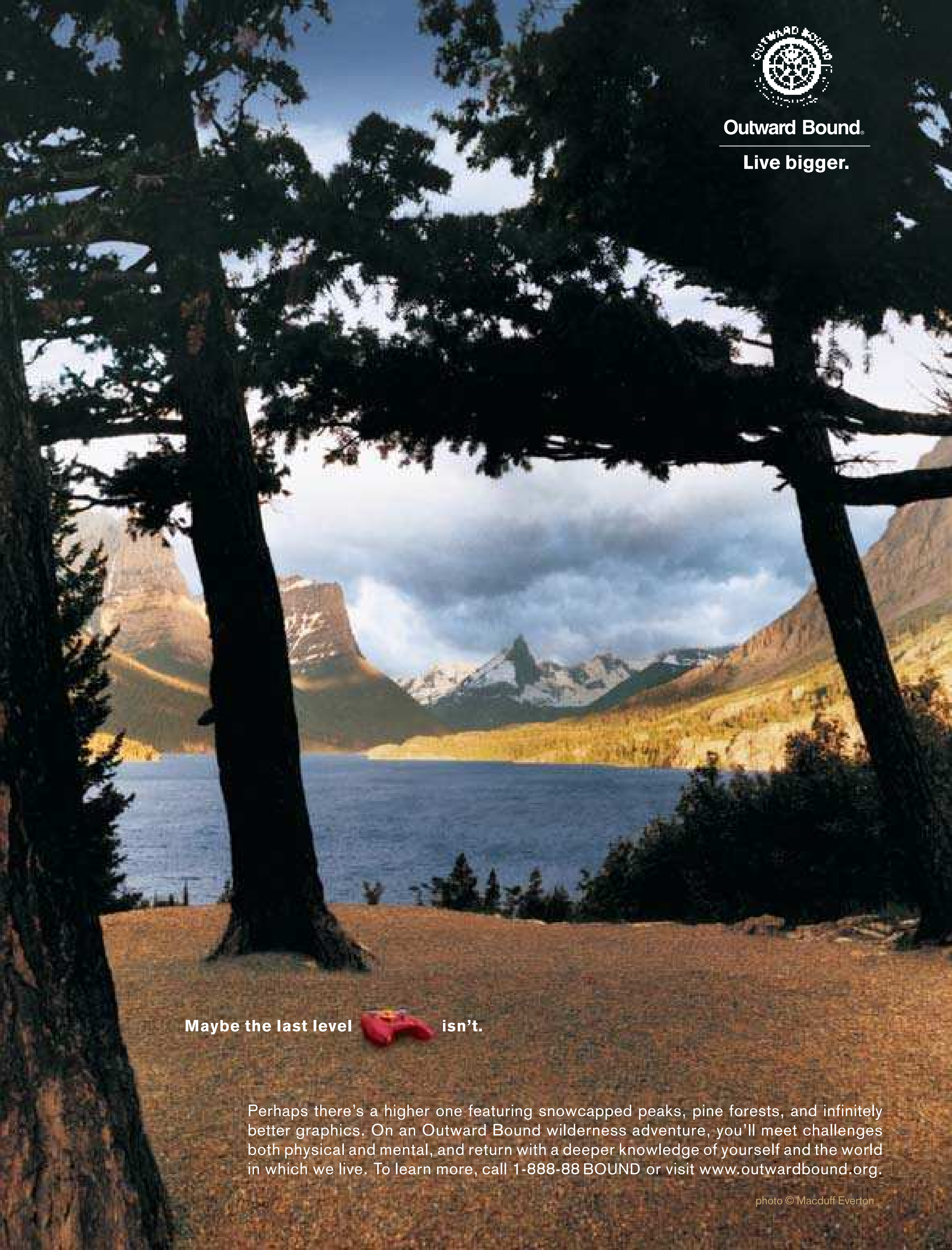
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